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THE POTENTIAL ENVIRONMENTAL CONSEQUENCES OF GENETIC ENGINEERING

HEARINGS

BEFORE THE

SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT

OF THE

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS UNITED STATES SENATE

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THE POTENTIAL ENVIRONMENTAL CONSEQUENCES OF GENETIC ENGINEERING

TUESDAY, SEPTEMBER 25, 1984

U.S. SENATE,
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS,
SUBCOMMITTEE ON TOXIC SUBSTANCES
AND ENVIRONMENTAL OVERSIGHT,
Washington, DC.

The subcommittee met, at 10:08 a.m., in room SD-406, Dirksen Senate Office Building, Hon. Dave Durenberger (chairman of the subcommittee) presiding.

Present: Senator Durenberger.

OPENING STATEMENT OF HON. DAVE DURENBERGER, U.S. SENATOR FROM THE STATE OF MINNESOTA

Senator DURENBERGER. The hearing will come to order.

Good morning everyone. Today and again on Thursday morning we will consider a subject that not very long ago fell into the realm of science fiction: the subject of genetic engineering and its potential consequences on our environment.

Genetic engineering is one aspect of the burgeoning biotechnology industry, an industry that uses and alters living organisms to create products. By manipulating genetic material, scientists can now deliberately redraw the fundamental blueprints of living things.

That is an awesome prospect. A chance to improve the quality of life worldwide. New bacteria that will clean up oil spills, produce rare drugs, and create super crops that resist disease and make their own fertilizer. What better use of science than to protect our environment, cure the sick, and feed the hungry?

We are enthusiastic and optimistic about this new technology, and we should be. But we are also a little wary and a little frightened. And I suppose we should be.

Do we really understand the consequences of these powerful new tools? In our haste to gain the obvious benefits, might we cause unintended harm?

Let me mention one example I have come across in my reading. Apparently scientists are working to create a bacterium that digests lignin, a component of plant cells that resists decomposition. If an organism can be engineered to break down lignin, then plant material will yield more energy in a biomass conversion system. We would be one step closer to an alternative energy supply.

But plants contain lignin for a very good reason. It helps them resist disease. And because it is so resistant to decay, lignin helps maintain the fertility in soil.

Shouldn't we think very carefully about creating a microorganism that could destroy the productivity of our agricultural soils?

I do not claim to be an expert on this particular case, and there may be good scientific reasons that make it perfectly safe. The point is this: A situation is developing in which our ability to mainpulate nature—to rearrange the building blocks of life—outstrips our ability to predict the consequences.

But that is always the way of science. The breakthrough comes, and we do our best to deal with the implications. That is why we have called these hearings: to begin asking the questions about the benefits and risks of this new industry to our environment.

I think you will find these hearings unusual. First of all, because the subject is an exotic technology that very few people—especially Senators—know very much about; and second, because our inquiry is prospective. All too often Congress acts in a sort of damage-control capacity, trying to solve or minimize an environmental problem that has already become major. This time we have a chance to prevent harm before it occurs.

I hope we can address some basic questions during these 2 days of hearings. First, does genetic engineering present the possibility of significant harm to the environment? And second, is the existing patchwork of statutes, regulations and guidelines adequate to prevent any potential problems? I understand the EPA will be issuing regulations before long to regulate the products of biotechnology under two existing toxic substance laws, and I will be interested to hear more on that subject.

In dealing with these questions, I would urge our witnesses to remember they are addressing a lay audience, so please try to keep the technical jargon to a minimum, if possible, and also please try to observe the 10-minute limit so that everyone has a chance to be heard this morning.

I appreciate the attendance today of all of our witnesses, and I will indicate in advance that their prepared testimony will be made a part of the hearing record if they choose to summarize.

I will call now our first panel: Dr. Bernard Talbot, Acting Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; Dr. John A. Moore, Assistant Administrator, Pesticides and Toxic Substances, Environmental Protection Agency; and Dr. Edgar L. Kendrick, Administrator, Office of Grants and Program Systems, Department of Agriculture.

We will proceed with Dr. Talbot.

STATEMENT OF DR. BERNARD TALBOT, ACTING DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH

Dr. TALBOT. Thank you.

I have been associated since 1975 with the original preparation and with all subsequent revisions of the NIH Guidelines for Research Involving Recombinant DNA Molecules. These safety stand-

ards were developed in response to a request by scientists that the NIH devise such guidelines.

Overseeing the NIH guidelines is the Recombinant DNA Advisory Committee, called RAC for short. The RAC consists of 25 voting members plus nonvoting representatives of many Federal agencies. The voting members include eminent scientists of many different disciplines, a lawyer who is the current chairman, a former State legislator, an occupational safety expert, a housewife, practicing physicians, and a bioethicist. Federal agencies with representatives on the RAC include the Department of Agriculture and the Environmental Protection Agency.

Since December 1978, the Guidelines have required that deliberate release into the environment of any organism containing recombinant DNA must have prior approval by the NIH, following review by the RAC, with opportunity for public comment and approval by the local institutional biosafety committee.

To date, three such cases of deliberate release have been approved by NIH. In each of these cases:

First, notice was placed in the Federal Register at least 30 days prior to the RAC meeting at which the proposal was discussed, giving notice and inviting public comment on the proposal.

Then the proposal was discussed at an open session of a RAC meeting, at which the possible hazards of the experiment were carefully considered. Following the discussion, the RAC voted in each of the three cases to recommend approval.

Advice was also sought from the Department of Agriculture Recombinant DNA Research Committee, which in each of the three cases recommended approval. And finally, NIH approved each of the three proposals with a notice in the Federal Register.

The three approved cases are: approval to Dr. Ronald Davis, of Stanford University, to field test corn plants transformed by corn DNA; approval to Dr. John Sanford, of Cornell University, to field test tomato and tobacco plants transformed with bacterial and yeast DNA; and approval to Drs. Steven Lindow and Nickolas Panopoulos of the University of California, Berkeley, to field-test bacteria carrying deletions in the genes involved in ice nucleation. None of these three approved field tests has actually been conducted to date.

NIH is not a regulatory agency and has no statutory authority over industry. NIH's mission is the funding of research, and it has authority to impose requirements only on those institutions which accept NIH research funds. Most private companies do not receive NIH funds and, therefore, are not required to comply with the NIH guidelines.

During the 95th Congress, in 1977 and 1978, 16 different bills dealing with recombinant NDA were introduced. Bills which would have made the NIH guidelines mandatory for the entire country passed committees in both the House and Senate but never reached the floor of the House or Senate for a vote. There is therefore today no national law making the NIH guidelines mandatory for private industry.

In the absence of national legislation, a number of localities have passed local ordinances making the NIH guidelines mandatory. For the rest of the country, other than these localities, for work not

supported by Federal funds, compliance with the NIH guidelines is not mandatory.

There is, however, a section of the NIH guidelines entitled "Voluntary Compliance" which encourages commercial organizations to comply voluntarily with the guidelines. At the last RAC meeting, two proposals for field tests of genetically engineered organisms, voluntarily submitted by private companies, were reviewed and recommended for approval. A final NIH decision on these proposals has not yet been made.

In September 1983, a lawsuit was filed by Jeremy Rifkin and others charging violation of the National Environmental Policy Act, and in May 1984, Judge John Sirica issued a preliminary injunction enjoining the NIH from approving deliberate release experiments submitted by NIH grantee institutions, although specifically allowing NIH to approve such experiments voluntarily submitted by industry. The Government is appealing the preliminary injunction.

In April 1984, the Cabinet Council on Natural Resources and Environment Working Group on Biotechnology was established. It consists of representatives of many Federal agencies. It is directed to undertake a review of the Federal regulatory rules and procedures relating to biotechnology, including a review of the function of the NIH Recombinant DNA Advisory Committee.

This concludes my prepared testimony. I will be pleased to answer any questions.

Senator DURENBERGER. Thank you very much, Dr. Talbot.

Dr. Moore.

STATEMENT OF DR. JOHN A. MOORE, ASSISTANT ADMINISTRATOR, PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY

Dr. MOORE. Thank you, Senator Durenberger.

Biotechnology is the application of biological science towards technological ends, such as the production or use of chemicals or life forms for commercial or potentially commercial uses. Recent developments in biological sciences have greatly enhanced scientists' ability to manipulate genetic material and to develop new microorganisms, plants and animals. These advances are expected to lead to the availability of a variety of useful products in a wide range of industries, including chemical production, agriculture and environmental protection. Commercial products of biotechnology are expected to be available in the very near future.

As with any new process, there are questions about the human health and environmental implications of developing and using microorganisms for commercial purposes. Novel microorganisms, whether they are nonindigenous or whether they are actually genetically manipulated organisms, may be placed in ecosystems where they have not existed before and where natural mechanisms for controlling their populations may not exist.

To address these concerns, EPA is developing a regulatory framework for reviewing certain commercial products of biotechnology that would come under our jurisdiction and review before they are intentionally released into the environment.

We will be invoking our statutory authority to review and, where necessary, regulate products intended for commercial use. We are not intending to arbitrarily extend our authority to all products or processes of biotechnology.

EPA intends to publish two Federal Register notices addressing EPA's statutory authority and planned regulatory approaches in this area. It is my understanding that other agencies that have regulatory authority in this field are also considering preparation of such guidelines.

The first notice EPA is going to be issuing will be an interim policy statement specifically dealing with the field testing of novel microbial pesticides which EPA is addressing.

We define novel microbial pesticides to be those which contain naturally occurring microorganisms for use in environments where they are not native, or microorganisms which have been genetically altered or manipulated by humans.

This interim policy will require a notification to EPA prior to all small-scale field tests involving deliberate release into the environment. This notification will permit EPA to determine whether an experimental use permit will be required before small-scale field testing is conducted. This interim procedure will not apply to studies conducted in contained experimental facilities such as laboratories, growth chambers, greenhouses or other facilities where there is no deliberate release into the environment. This notification procedure will allow the agency to evaluate the potential risks of field tests with only a minimum impact on the development of beneficial novel microbial pesticides.

The second and more general Federal Register notice will discuss the Agency's broad policy regarding the regulation of novel microbial products under TSCA and FIFRA. This notice will clarify EPA's regulatory authority over novel microbial pesticides and will outline the agency's specific plans for reviewing and registering these pesticides under FIFRA.

The notice will also discuss EPA's proposed policy for reviewing novel microbial products under TSCA. In particular, EPA believes that novel microbial products produced by recombinant DNA, cell fusion, or other techniques of genetic engineering are new chemical substances subject to the premanufacture notification requirements, unless they are substances such as drugs or pesticides that are excluded by statute from TSCA regulation.

The agency also intends to address the applicability of TSCA requirements to field tests or other research and development activities. The notice will provide an opportunity for public comment on how the agency should apply these two statutes to novel organisms. Although a large volume of comments is anticipated, we commit ourselves to expeditiously review these comments and promulgate the final policy quickly and prudently.

EPA's Office of Research and Development is conducting important research in the area of biotechnology to address three important issues: (1) The possible public health and environmental consequences of the release of novel microorganisms into the open environment; (2) the possible consequences associated with the increase of wastes and emissions from a growing biotechnology industry; and (3) the application of biotechnology to improve the environ-

ment by degrading persistent and toxic chemicals to provide previously unavailable tools for monitoring pollutants.

ORD has already sponsored workshops consisting of scientific experts in this area from academia, industry and Government to identify the major areas where knowledge is lacking and to define further the Agency's research plan.

The consensus of these workshops is that considerable information already exists which is relevant to the assessment of microbials. The recommendations were that this information needs further review and should be built upon in the future to address information gaps and standard protocols that are currently unavailable.

To ensure that the workshop recommendations and EPA plans are appropriately developed, a biotechnology research program management team has been formed to coordinate activities within ORD and to facilitate responses to regulatory office needs.

Obviously, a major issue in any regulation of genetically engineered organisms is the effect of Federal oversight and regulation in innovation in what is a very promising industry. Innovation is likely to be of major economic importance to the U.S. economy and to provide significant benefits to the public. Unnecessary or confusing regulations will pose a serious problem to industry and may give a competitive advantage to those in foreign countries.

The biotechnology field is in its infancy and our regulatory framework must be flexible to allow the evolution of policies as new knowledge becomes available. Thus, it is also essential that the Federal Government coordinate its efforts in regulating this new industry and ensure that any regulations imposed are necessary, consistent, and appropriate.

As the subcommittee is aware, the Administration has formed an ad hoc working group of the Cabinet Council on Natural Resources and the Environment to address Federal regulation in this area and to ensure a consistent overall approach. EPA is an active member of the working group. EPA is also working closely with other Federal agencies that share an interest in biotechnology, including the National Institutes of Health and the Department of Agriculture.

I believe that a coordinated Federal approach in this area involving all interested agencies will permit a highly successful biotechnology industry to exist in this country, while at the same time ensuring protection of public health and the environment.

That concludes my statement, Mr. Chairman.

Senator DURENBERGER. Thank you, Jack.

Dr. Kendrick.

STATEMENT OF DR. EDGAR L. KENDRICK, ADMINISTRATOR, OFFICE OF GRANTS AND PROGRAM SYSTEMS, DEPARTMENT OF AGRICULTURE

Dr. KENDRICK. Mr. Chairman, thank you for the opportunity to testify on the role of the U.S. Department of Agriculture on the subject of this hearing.

The Department of Agriculture has had responsibility since its founding over a century ago to sponsor research and encourage the application of this research for the betterment of the food, feed,

and fiber needs of the Nation, in both its national and international roles.

At its founding, the Department was also uniquely enjoined with the land-grant university development and, as a result, the research and application responsibility is fulfilled through State, Federal, and private cooperative efforts.

We believe this vast network of scientific expertise, laboratories and controlled environmental facilities have indeed provided well for the nation in the past, and with our careful planning and introduction of the new biotechnology initiative, including genetic engineering, we will be able to continue to serve the Nation in the future.

I recognize that this subcommittee's immediate interest is in what is commonly referred to as genetically engineered organisms, and most especially wherein recombinant DNA technologies have been utilized in plant, animal or microbial species, and deliberate or intentional release of the improved species is desired. However, as background, I think it is important to note that the agricultural research community has had a long and highly successful history of developing the genetic components of plant, animal and microbial life for the benefit of society and its environment broadly.

All the major animal and crop species used for agricultural production in America today have been critically designed and deliberately released. Also, millions of acres of trees are similarly designed to provide our fiber needs. In total, these food, feed and fiber production processes involved deliberate release into the environment of billions of living organisms, each involving design and manipulation of their DNA components 'The corn crop alone this year has been estimated to have $193x10^{10}$ plants, or 193 trillion, each with its own designed DNA components. Not only did the total agricultural mass of living organisms interact with existing organisms in the environment, it also withstood an array of natural and manmade threats while contributing vastly to society's well-being. Its complexity is staggering.

Recombinant DNA, and other closely related genetic engineering policy issues, are addressed by the USDA Recombinant DNA Research Committee, known as ARRC. Research in laboratories and other controlled environments, as well as release into the environment broadly, is critically assessed. Each agency in the Department that is directly concerned with recombinant DNA research and its application and regulation is represented on our ARRC. In addition, the Director of the Office of Recombinant DNA Activities of NIH, which administers the Recombinant DNA Advisory Committee, RAC, and the guidelines, is also a member of our committee. Similarly, a National Science Foundation representative is also a member of our committee.

Other research policy committees concerned with recombinant DNA and the new biotechnology in agriculture include the Experiment Station Committee on Organization and Policy, ESCOP, and the Committee on Biotechnology of the National Association of State Universities and Land Grand Colleges, NASULGC.

In the evaluation and review of research involving recombinant DNA, including field experiments, the Institutional Biosafety Committees, IBC's, are an essential feature. This is so both in Federal,

State, private and industrial facilities. The IBC's are an essential feature of the RAC and guideline processes.

At the earliest stages of development of RAC and the guidelines for conducting recombinant DNA research, USDA scientists and scientists from the agricultural research community broadly were involved. Along with the scientific community, we have strongly supported the concept of a set of standards and procedures for the conduct of recombinant DNA research in the United States. We remain highly supportive of RAC, and scientists from the agricultural research community serve on the committee and on special working groups constructed by the committee as needed. The ARRC was designed to be complementary to the RAC processes and is so utilized today. Projects and policy issues involving agricultural interests are reviewed by ARRC on behalf of RAC and in furtherance of the guidelines processes.

In the Department and in the scientific community we find in place mechanisms that provide continual review and oversight of research as new knowledge evolves. These mechanisms also provide for special considerations warranted by genetically engineered organisms.

We highly applaud the RAC process. With a decade of experience we find it has earned wide respect over the Nation and the world. Concepts built into the processes early on provided for change as knowledge overtime was acquired and attracted the highest levels of expertise. A highly participatory process with a full range of expertise and interest all have contributed to its success. These check and balance processes have assured that it is not self-serving, but has addressed the needs of society broadly in this area.

Research projects that envision potential release into the environment under controlled research conditions, or ultimately broad release, have built into them at an early stage extensive study and review of the molecular ecology involved. Furthermore, biological containment and gene performance in increasingly complex environments are tested under controlled conditions. Specific environments, genetic drift and gene wearing in mixed systems are tested under controlled conditions. The multitude of naturally occurring genetic accidents and the resulting potential for interaction, as well as ecological gene training and attenuation, are similarly tested.

Thus the resulting plant, animal, or microbial biota to be used in agriculture, wherein recombinant DNA technologies have been employed in their development, are not inherently different in nature than those we have used in the past. These resulting products should not be treated differently.

In summary, I have outlined the evaluation and oversight activities involving research and field experimentation with genetically engineered organism.

This completes my statement. I will be pleased to answer any questions.

Senator DURENBERGER. Thank you very much.

Jack Moore, you have been here more often than the other two, so I will start with you.

The very fact EPA is spending a lot of time working on a regulatory program tells me that you think there is in fact a potential for

adverse environmental effects. I wonder if you would indicate to us what you see these effects to be and what you will be looking for when you review and experiment on the product.

Dr. MOORE. Senator, let me respond by selecting a few things out of the interim Federal Register notice which deals with novel microbial pesticides; this notice should be signed and available within a few days.

Chemical pesticides have no independent mobility or reproductive capability. Microbial pesticides, on the other hand, may replicate and may spread beyond the site of applications. As I mentioned in my opening statement, microbial pesticides may not be subject to natural control or dissemination mechanisms. Therefore, small-scale field studies with novel microbial pesticides can raise many of the same concerns as the more extensive use of conventional chemical pesticides raises. This is why we want to get at them early. I think it also intimates as to what is the nature of some of the concerns that we have.

At present, there is a high degree of uncertainty in predicting the ecological impacts of releasing the microbial pesticides into the environment. For example, novel microbial pesticides could exhibit increased competitiveness, a greater ability to survive, broader host range, enhanced virulence, compared to the indigenous microbes, or its introduction could lead to ecological perturbalions.

Because microorganisms can reproduce and be disseminated by a variety of different mechanisms, they may be difficult to control or eradicate after being introduced. Therefore, I think what we are looking for in the way of evaluating such material before it gets into the environment, even under an experimental use permit for pesticides, is "Will it stay where it is going to be put?" Is it host specific—obivously a pesticide is developed to do something that we think is desirable—what else might it do or, indeed, is it only going to do that which is intended? How long will it remain in the plant or soil, or whatever the case may be? It is these types of activities we are interested in.

We are also interested as to whether or not it can cross-infect or trade, if you will, some of its new genetic information with indigenous plants. We are trying to identify the need for test data and approaches to test data that will give us information so one can make an informed opinion as to whether or not one wants to go ahead with the uses.

Senator DURENBERGER. Dr. Kendrick, I always hate to characterize people's testimony, but you seem to be saying that the new genetic engineering technologies aren't really the science fiction that I referred to in my opening statement, nor especially exotic, but just another example of the genetic manipulation that has been going on in agriculture for a long time. Do I understand that to be an accurate characterization?

Dr. KENDRICK. That would be accurate.

Senator DURENBERGER. Let me then read to you a few lines from a recent issue of Omni magazine.

Using a new heat-shock process, Barry McDonald and William Wimpey have fused cow cells with cells from a tomato plant, creating a typical-looking tomato plant with tough, leatherlike skin.

According to A. DeMaggio, a plant development physiologist at Dartmouth College, this type of work is going on in several laboratories around the world.

McDonald and Wimpey, encouraged by their initial success, have embarked on a new project, aimed at producing a tomato-wheat-cow superhybrid. With the soaring costs of raising cattle, the researchers hope to develop an easily grown, protein-rich "plant"for production on "wheat ranches."

I am just wondering if that sounds to you like traditional breeding practices.

Does the USDA review system contemplate an ability to handle research of this type?

Dr. KENDRICK. Yes, I believe we could. What you have cited is an ability, in my opinion, of a technology that now allows scientists to go in and extract specific genes and insert them in the organism that they want to, for improvement of that organism.

Triticales is a product of wheat and rye, two species that do not cross naturally. However, through genetic manipulation, mutagenesis, and so forth we came up with a product of these two species, Triticales.

So I believe that is not the traditional breeding that you cited; but there are going to be desirable genes in other organisms that do not naturally cross, that will be investigated and inserted into certain organisms for their improvement.

What I am saying is we have a system; we have people who understand all those specific organisms and can follow and, test them responsibly.

Senator DURENBERGER. Why don't you give us, without a lot of detail, a brief explanation of how you have changed the people in the technical capacity within USDA to handle this somewhat different research.

Dr. KENDRICK. I am not sure that we have. If I understand your question, Senator, how we changed the ability?

Senator DURENBERGER. Even I can understand tomatoes and wheat, but when you start adding cows and some of these other things, it strikes me that perhaps some of the scientific expertise that you might require to do a review system might change. I am wondering about the degree to which you have changed that capacity in terms of personnel.

Dr. KENDRICK. I think we have the existing scientific expertise on board and accessible to us, through the vast land grant system and the Agricultural Research Service. We can go to these people. I believe that the Institutional Biosafety Committees that I mentioned would be operative in overseeing the kind of research that you just cited. They would first review that kind of research, if it had not previously come to the RAC. Thus, there would be some people that are very broadly knowledgeable, as the people are who serve on the RAC, who would be looking at that experiment before it was ever carried out.

Senator DURENBERGER. I am given to understand, and I have no independent means of verifying this, that a lot of the new genetic engineering biotechnology companies that are rising have arisen from the genius of, among others, land grant university scientists who either deliberately or accidentally stumbled across a variety of new opportunities, and they sort of spin themselves out of a low-

paying environment into an opportunity that all of us, of course, may envy.

Do you see in your reliance on university-based research and review any potential conflict with the USDA review process? Obviously what I am getting at is the question that is always raised with regard to USDA: Is it in the promotion business or what business is it really in; and to what degree, if we are looking at this in terms of societal safeguards, can we rely upon the USDA review process?

Dr. KENDRICK. Our committee in agriculture is very heavily science based. At the recent Biotech 84 conference, I think this very issue came up, about all the experts are going to be over there in the biotech industry where perhaps the greater opportunities are for reward and the like.

I think the academic community feels this as do some of the people who are now practicing biotech in industry, that there are going to be those people who would rather remain in academia and who will continue to serve on committees like the RAC and who will be accessible to our agriculture committees. So we think it will continue to be not a self-serving process.

I know what you are referring to, that we will be looking out strictly for the interests of agriculture. But our committee is trying to make its decisions based on good science.

Senator DURENBERGER. The traditional process is, as a new industry develops, it calls upon some very talented people from universities, for example, in a consultant capacity to advise these emerging industries.

To what degree, or maybe it is too early to tell, are some of these consultants that are used by you in your review process also used by some in the promotion of product development in the private sector?

Dr. KENDRICK. There are many of them, as you have indicated, that are serving in the dual roles: remaining with the academic community and in a consulting role with the industry.

In our review process we, of course, will try to not rely too heavily on that person who has the dual association because we recognize we are a public agency. So there doesn't appear to be that conflict of interest, we will try to rely primarily on those who are the pure academic types. I believe there will continue to be some of those. Also I believe we will want to work with those people out in the industry who are at the forefront of what is going on and we will want to have some exchange with them. We will not rely on them that heavily or totally in the review process.

Senator DURENBERGER. Dr. Talbot, you point out in your testimony that private industry does not have to submit release experiments to RAC. That is a correct statement of your testimony, is it not?

Dr. TALBOT. Yes.

Senator DURENBERGER. As your testimony indicates also, two or three companies have done so. I think the first three were voluntary submissions. The committee recommended approval of all three. I am not clear whether the Director of NIH has acted on any of them.

Dr. TALBOT. We have had numerous submissions from private companies in other areas than for deliberate release to the environment. But my testimony concentrated on deliberate release to the environment of organisms containing recombinant DNA. In that area, NIH has approved three proposals, all of which came from academic institutions which are required to submit because they are receiving, their academic organizations, NIH funds for recombinant DNA research. That is Cornell University, the University of California at Berkeley, and Stanford University.

At the last RAC meeting the RCA Committee took up two proposals voluntarily submitted from private companies for deliberate release to the environment of organisms containing recombinant DNA. NIH has not yet made a decision on those.

In other areas not dealing with deliberate release there have been numerous submissions from private companies and numerous questions from private companies asking for interpretations of the Guidelines and registering their local Institutional Biosafety Committees with us and checking if they meet the criteria of the Guidelines.

Senator DURENBERGER. Is there any Federal law or regulation that would prevent companies that may have submitted voluntarily but who get tired of waiting for the Director to make a decision to just go ahead with their experiment?

Dr. TALBOT. There is no law or regulation prohibiting them from going ahead if they get tired of waiting.

Senator DURENBERGER. I heard reports that one of the three voluntary submissions has made inquiries of the Canadian Government about performing the experiment in Canada instead of the United States. Do you know anything about that?

Dr. TALBOT. I have heard that third hand and not directly. I have not verified that directly.

Senator DURENBERGER. You mentioned one limitation of the NIH guidelines, that they have no regulatory force over many of the experiments that may be of concern. Isn't there also a second limitation, that your guidelines apply only to recombinant DNA experiments, not to fusion or other forms of genetic manipulation?

Dr. TALBOT. That is correct.

Senator DURENBERGER. Dr. Kendrick, you mentioned a number of review safeguards that are applied to genetic engineering which left me with the impression that each release experiment is thoroughly scrutinized before it is carried out. Do private genetic engineering companies have to get a USDA clearance through this review process before they carry out a release experiment?

Dr. KENDRICK. No; they do not have to get a permit from the USDA.

Senator DURENBERGER. So then who is subject to the review process?

Dr. KENDRICK. So far we have been implementing the recombinant DNA guidelines, and all of our people in the Federal Government, all Federal research scientists, must adhere to those recombinant DNA guidelines, also anybody who has a cooperative agreement with us through some Federal funding.

Let me give you an example. We are working through these things right now with regard to our existing regulations, which are

housed primarily in the Animal and Plant Health Inspection Service. We are working through how we would handle these things that are coming about by means other than recombinant DNA to see whether we would need to modify the existing regulations.

Let's say Pioneer Hybrid wants to release a new corn plant that has a new resistance capacity which was achieved through other than recombinant DNA technology. If it had been recombinant DNA, it may or may not have come through the RAC.

Before Pioneer can put that new variety out on the market, it will be extensively tested. They will put it into the land grant testing system voluntarily. They always have and they will continue to do so, to see how it tests out against existing varieties. They will want the public sector to test that.

That is an experimental and a somewhat confined and controlled test. Then, before they release that variety in the State where they want to market it, they are going to have to deal with the regulatory authorities of that State. So it gets some sort of test and close scrutiny, along the way. They will have to identify what is new and novel, about that variety compared to some other varities that are in production. They will have to reveal to some extent, how did they arrive at that new genetic type.

Senator DURENBERGER. Is voluntarism in the area which Agriculture would be most concerned with—maybe you could just describe for us the traditional nature of voluntarism in complying particularly with some new Federal standards, or even if there aren't Federal standards or regulatory requirements. Is there a tradition of voluntarism on the part of the seed industry? You used Pioneer as an example. Are there some special reasons why in order to market a product against competition, or whatever, that you can have a degree of reliance on voluntarism in that particular part of the industry?

Dr. KENDRICK. Yes; I believe you described it right. There is a traditional and historical voluntarism. If they want to market that product, they will run it through the evaluation system that we have traditionally followed in agriculture, be it private industry or a public released variety. So pretty much in the seed industry I would say yes, it has been voluntary and will continue to be so.

Senator DURENBERGER. I don't know whether you are the person to answer this question, but I assume that to a degree either voluntarism or something else as you might characterize it has been true in the area of pesticides and insecticides for a long period of time. And to date, at least in the last year or so, we have found some reason to be concerned, not about the nature of the approval process or the regulatory requirement but the results of that process.

In other words, the impetus, obviously, is on expanding production by limiting the adverse effects of pests and insects and so forth. So, at least as I recall from our series of walking through the fields of ethylene dibromide, it looks like it is not a very complicated process to get USDA on your side, as you are marketing to farmers all over this country those kinds of new products that will increase their production in one way or another.

Have you seen that process change in the last year or so? Have you seen the attitude, if you will, on the part of the private sector industry toward the adequacy of the governmental processes to

react appropriately to the environmental concerns that their products might present? If you have, I wonder if you would share with us the nature of that change.

Dr. KENDRICK. Jack Moore, I am sure, may also have a comment on whether this attitude or willingness on the part of industry has changed with regard to testing pesticides, etc.

Let me say at the outset we fully recognize the role of EPA in the regulation of pesticides. We are not in the business to regulate pesticides in the Department of Agriculture, but we are involved in a lot of the experimentation and testing up to the time they are ready or being put out as a product.

Also, I would like to comment on your term, that we are trying to do these things to expand production; not necessarily to expand production. In fact, primarily, we see these tools that are in our hands right now, as giving us a great opportunity to increase productivity. Productivity means reducing farmers costs by using fewer pesticides which also helps reduce pollution. The benefit is there when he doesn't have to apply the expensive nine pesticide treatments. In other words, come up with new resistance, come up with a new way of controlling the gypsy moth or pests like this where you don't have to use the pesticides but rather use some means of biological control.

I want to make it clear that we are not looking only for ways to expand production. Production is not a real problem for us right now, as you well know.

Senator DURENBERGER. You mean 193 trillion corn plants is how many too many?

Dr. KENDRICK. You know, we had a shortage not too long ago. There will be people who will tell you we will have more shortages. So it is that ability, that capacity to produce that is important. We must continue to improve our ability to market this production.

Senator DURENBERGER. I clearly agree with you that maybe productivity is the better word. It is certainly appropriate if we are ever going to develop an agricultural policy in this country. If we restrain the expansion of the land base under that production, that we put much more of an emphasis on natural resource conservation, and that should logically lead you to get greater productivity out of a smaller natural resource base, which again brings me around to expressing my concern, as I have in these other questions, about the role that USDA plays in promoting productivity then will play in any kind of a review process that will substantially increase that productivity.

Dr. KENDRICK. I didn't directly answer your question about do I see an improvement or change in the private industry with regard to their wanting to test and evaluate these products. I believe yes, there is an awareness and a real sincere effort on their part to test more thoroughly than ever before.

Also, let me say that we in USDA recognize there are some people out there who see this as a real unknown, kind of a scary area, because we have these tools now and the ability to genetically engineer. What we want to convey, and we are in the process of trying to do a better job of that than we have done, is that we have been genetically manipulating plants, animals, and microorganisms for years in a less precise manner than we are able to do now. It is

happening in nature every day, and we have a lot of people that have followed that process very closely; people who work on nothing but one type of bacterium, one species of bacterium, and who are pretty knowledgeable of all of the variants that exist in that bacterium. They have studied its ecology. They can predict pretty well what will happen with that organism.

So we want to assure people of this evaluation and testing procedure that we have followed for years and convey to them that we really don't see any great danger. However, we recognize it is an unknown to some people right now. Thus, we are in the process of trying to more clearly articulate our rules and regulations, our oversight.

We want to work with the EPA and the NIH in their roles. We think we will do a better total job that way.

Senator DURENBERGER. Jack, I wonder if you would add a dimension from your point of view to the question I raised relative to the private sector. It seems to me that in the last 6 or 8 months, the food processors are pretty dissatisfied with the way we in government, over the years, have approached this whole business of environmental safeguards when we in effect put our good government seal of approval on these products.

It seems to me that they are looking to us now, particularly as we enter into an exciting new field, for some clear guidance and sense of direction before we encourage another industry to improve the quality of our life.

I wonder if you might just react to that change, if, in fact, it exists out there.

Dr. MOORE. I might make two comments. My perception is similar to yours as it relates to the food processing industry. That is that in the last 6 or 8 months, they certainly have developed a very keen interest and awareness as to what EPA might be doing or might not be doing in the area of pesticides as it might relate to their ability to do business.

This awareness I think is a very productive one as opposed to being an adversarial type of relationship. They have had discussions with us, for example, as to what are we planning to do in the interim? How might they help us? What data do they have that might allow us to make a more informed judgment on something that is a prospect?

The other aspect, and I am not sure this reflects any rapid change in perspective—it might reflect a learning curve on my part—is the farm user, if you will, of pesticides certainly has a broader perception of what he or she wants to do than maybe I was willing to give them credit for. They are certainly aware of the need for integrated pest management or the need for other types of practices which might reduce their reliance on chemical pesticides of one sort or another. One, because of cost; but I think even cost aside, the other thing that strikes me is that they are fairly well up and abreast on integrated pest management: for example, that there are alternative ways that they might be able to achieve some of their ends which allows them to reserve or preserve, if you will, the effectiveness of the pesticide.

No longer, I think, are you seeing farmers routinely using a pesticide over and over again. I think they would much rather use it

more as a scalpel type of approach as opposed to the shotgun type approach. So, I think they have learned from looking at the pesticides that first came on the market, where resistance developed, for example, where it was no longer available to them, not necessarily because the government took it away from them, but it just wasn't effective. They find if they can mix their pesticide control in one way or another, they are better off in the long run.

Senator DURENBERGER. You indicated in your testimony, Jack, that the testing requirements will allow the Agency to evaluate the potential risks of field tests with only a minimum impact on the development of beneficial novel microbial pesticides.

I wonder if you would elaborate on that.

Dr. MOORE. Yes; section 5 of TSCA exempts new chemical substances that are produced in small quantities solely for the purposes of research and development. In looking at that approach as it relates to biotechnology and the development of microbial pesticides, there may be a need for us to better define by rule what we mean by small quantities and, indeed, the possibility might be to take out from this PMN notice exemption microbial pesticides that are destined for environmental penetrants as a part of their R&D process, again falling on the logic that if you don't, there, indeed, may be an adverse effect where none was anticipated, and it won't be captured by the PMN process.

Senator DURENBERGER. Part of the problem is distinguishing from the purpose, whether it is R&D or being manufactured for commercial purposes. Can you address that by rule or would it be helpful if, as we approach TSCA amendments, we clarify that authority?

Dr. MOORE. Our current feeling is that we ought to try to see if we can do it by rule. I don't foreclose the need for possible statutory assistance. But right now we have some degree of confidence that at least from the standpoint of somebody who is undertaking an R&D effort for commercial purposes, we might be able to close that exclusion by saying that novel microbial products are excluded from this R&D exemption.

Senator DURENBERGER. Your testimony also notes problems that might arise from release of genetically manipulated organisms. Yet, some people argue that making genetic changes in native organisms is not risky, at least not as risky as introducing a nonindigenous or exotic organism.

Is EPA going to make any distinction between native species and exotic species where genetic engineering is concerned, or do you think such a distinction even warranted?

Dr. MOORE. No; I think we are looking to apply to TSCA the same logic we have applied to FIFRA. That is, a novel microbial in this case is not necessarily one that was created just through genetic manipulation but, indeed, might also be one created by finding something that was 'natural' in its occurrence and putting it in an unnatural place.

Before one allows that, if that unnatural place is out in the environment, I think again we need to have some sense of what are the normal controls that are out there that might make sure this thing does what it is intended to do and doesn't do anything we don't want it to do.

Senator DURENBERGER. On the subject of the Cabinet Council that all three of you referred to; how is this particular biotechnology subcommittee being staffed?

Dr. MOORE. Participation by a wide variety of agencies. I am not sure I could list them all.

Senator DURENBERGER. Is there a lead to the process? Just tell us something about how it is operating or going to operate.

Dr. MOORE. The work group is chaired by OSTP. Jay Keyworth is chairing the effort.

One of the first things that has been done is there has been a collation of all of the statutes that have some bearing on biotechnology and an analysis on the basis of the feeling on the part of the respective agencies of how their particular statute may be appropriate and how they are using it or plan to use it.

There is an intent I believe this fall to publish that in the Federal Register, which would help other communities in general to know who has what role under what circumstances.

Also, in the process of doing this, one underscores, if you will, areas of overlap which should be reconciled prospectively, as well as gaps that should be discussed.

I think the more important thing we are also trying to do in that effort is to see if indeed one can come up with a general approach which a number of the agencies can utilize rather than each of us going off, such as little fiefdoms might do, and recreate the wheel over and over again, which I don't think benefits anyone.

Senator DURENBERGER. I take it, Dr. Talbot, that you are comfortable that others representing the Government are now getting into this area and looking at it from a variety of more appropriate standpoints.

Dr. TALBOT. Very much so.

Senator DURENBERGER. I also get the impression, given the basic charge of NIH and the vital function that it has to play in our society, that you probably wouldn't mind being relieved of the sort of quasi-regulatory role in which you have found yourself, at least insofar as it relates to environmental release; is that correct?

Dr. TALBOT. I think there are many at NIH who would look forward to our getting out of some of these roles we played. The Cabinet Council Working Group is looking at this and will be presumably coming up with a plan that Jack Moore has alluded to which would perhaps take certain functions away from NIH, or perhaps even add additional functions to NIH. Until they have reached a conclusion as to the overall need for a risk assessment strategy for the whole Government, we are not really sure what that biotechnology working group will come up with.

Senator DURENBERGER. Thank you all very much for your testimony. I appreciate it a great deal.

Our second panel is Dr. Alexander MacLachlan, director, of central research and development department, E.I. du Pont de Nemours; Dr. Martin Alexander, professor, department of agronomy, Cornell University; and Dr. Winston Brill, vice president, research and development, Agracetus Corp.

Gentlemen, we appreciate your being here and your patience through the last hour. As I indicated to the other witnesses, your statements, which we appreciate your preparing in advance, will be

made a part of the hearing record in full and we would appreciate your summarizing.

We will ask you, as we have asked the other witnesses, to keep your terminology to understandable for the generously called laypersons at this table. Please limit it to 10 minutes in summary.

We will start with Dr. MacLachlan.

STATEMENT OF DR. ALEXANDER MacLACHLAN, DIRECTOR, CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT, E.I. DU PONT DE NEMOURS

Dr. MACLACHLAN. Good morning. I am Dr. Alexander MacLachlan, director of central research and development department, du Pont. This department does most of the long-range basic research for the company and also introduces new technologies. One of the most important at the present time is biotechnology. My remarks will deal with du Pont's involvement in the new biotechnology and our views on how the Government should regulate it.

As you know, I have submitted a longer statement which should be made part of the record. This is just a summary.

For clarity, let me define what I mean by biotechnology. Biotechnology is the directed molecular restructuring of genetic material often referred to as genetic engineering. This test-tube splicing of DNA and its introduction into cells is in direct contrast to more traditional ways of moving genetic material around, such as plant and animal breeding.

From a business point of view, du Pont already has a major stake in the life sciences where biotechnology will make its greatest impact. Although we have life sciences related sales at a level of about $2 billion in pharmaceuticals, radio pharmaceuticals, x-ray products, diagnostics, and agrichemicals, we do not yet sell any genetically engineered products.

However, at du Pont over the past 5 years we have invested over $150 million in new facilities, a large portion of which supports our research in the new biotechnology. Through biotechnology we seek understanding of disease and plant processes that we hope will lead to improved pharmaceuticals, diagnostics, and agrichemicals. These new products may be based on conventional chemicals or be derived or manufactured by processes based on biotechnology.

By any measure, du Pont has a major stake in biotechnology. But we are certainly not alone. Such commitments have been made broadly by American industrial concerns both large and small. The magnitude of this commitment combined with a scientific base second to none in our universities has given the United States its present leadership in the development of this new technology.

With this as background, let me summarize our views on Government regulation.

First, we believe that regulations governing the introduction into the environment of genetically engineered products, and their manufacture and distribution, are inevitable and should be implemented.

Second, as the regulations are implemented, it is important to distinguish between control of science and the regulation of products. Basic laboratory science should not be controlled beyond the

precedents established by the National Institutes of Health Recombinant DNA Advisory Committee, called RAC for short.

RAC has worked well. Its case-by-case examination by acknowledged experts is a sound basis of ensuring public and environmental safety.

While RAC guidelines are adequate for basic research, RAC does not have the resources to oversee the development of biotechnology products. Today, product developments arising from biotechnology have no clear regulatory oversight agency. We should not leave this vital new industry in such a limbo where laws and regulations developed for other purposes will be applied wihtout any understanding of the technology involved.

We believe this must be corrected at the earliest possible moment, and we believe that it can and should be done by existing Government agencies; specifically, the FDA, the EPA, the USDA, and OSHA. Several of these agencies believe that existing law gives them such authority, and we see no reason to challenge this.

What we do suggest is that there be a systematic coordination of regulatory oversight authority among these agencies. This coordination should involve several activities. Let me summarize what we believe they should be.

First, there should be a clear expression of jurisdiction by the involved agencies. Otherwise there may soon be a confusing array of overlapping regulations both at the Federal and State level.

Second, the agencies should establish guidelines based on the latest scientific information. This would form a consistent basis for administrative regulatory oversight. To do this the agencies must develop scientific competence in biotechnology. Until this is accomplished RAC should be consulted.

Third, we recommend establishment of an interagency committee for biotechnology regulation assessment. This committee would serve as a sounding board for those regulated as well as environmental and other citizens' groups and would be in a position to correct redundancies. This committee should exist for a finite term and only be appointed to another term if need dictates.

Fourth, we recommend that an eminent individual with broad background in biotechnology be appointed special counselor to the President for biotechnology. Such an office would ensure that emerging needs of this dynamic new technology are heard at the highest levels of Government.

Finally, there should be a strong commitment to retain RAC to continue to oversee laboratory research. RAC proceedings represent an important intellectual and scientific resource, and as new regulations are proposed, it would be unwise to part from its counsel.

In closing, we believe biotechnology will and should be regulated. We believe this should be done at the Federal level and we urge that the agencies involved clarify their oversight responsibility at the earliest time. We also urge that regulations be formulated with the continuing counsel of those at the leading edge of this technology. If we do this right and devise realistic and enlightened rules, we will give the public the best chance to benefit from this marvelous new technology.

Senator DURENBERGER. Thank you very much.

Dr. Alexander, you're next.

STATEMENT OF DR. MARTIN ALEXANDER, PROFESSOR, DEPARTMENT OF AGRONOMY, CORNELL UNIVERSITY

Dr. ALEXANDER. Mr. Chairman, I will shorten my lengthy written transcript given the constraints of time.

The introduction of a radically new technology usually will have a number of uncertainties associated with it. This probably has been true of every markedly new technology, whether it was the use of fire by primitive societies, the industrial revolution, or the application of nuclear energy to peaceful pursuits.

The proponents of these technologies, probably in the past and certainly at present, argue for the enormous potential benefits and the absence of uncertainties. These proponents are undoubtedly among the best spokesmen for the benefits; it is their field.

However, it does not necessarily follow that those that know a technology can also assess its risk. These individuals understand their technology and have much to offer to society by exploiting it, but one should clearly distinguish their knowledge of how to make use of a particular technology and the information needed to assess the risks from what they plan to do.

For the environmental scientist, which I am, there is a high degree of uncertainty in anticipating the consequences of genetic engineering. Uncertainty is not equivalent to a belief that there is, or will very soon be, a problem, but it is associated with a feeling that we are progressing along a course of action that may lead to minor or major problems in the near or in the long term.

If genetic engineering is indeed the wonderful technology that many of us believe, it will be used in ever more numerous ways, and the various approaches currently being developed will be expanded to include a variety of organisms, uses, and environments.

It has been stated frequently that no problems have arisen with the few techniques and few organisms that have been engineered to date, but the ever-expanding scope of genetics and the new areas for practical exploitation will take us far beyond these few techniques and these few organisms.

In this light, I, as an ecologist, am not too bothered by the lack of information on the possible environmental consequences of the still infant field of genetic engineering. However, I am enormously concerned by the lack of a meaningful base of information to predict what might occur as the science develops and industry becomes able to transfer an increasing amount of genetic information from one of many organisms to a variety of other organisms.

It is the ever-growing number of organisms and the diversity of techniques that will be used in genetic engineering that increase the concern about our uncertainties and our lack of information.

Natural environments have a variety of checks and balances that prevent the many species and populations in our surroundings from being overly abundant or doing major harm to other species. It is these very interactions that prevent most organisms from one habitat from becoming established in another.

These same mechanisms probably will destroy most of the engineered organisms that are deliberately introduced, just as they

have eliminated most organisms that are transported from one environment to another. Because of these natural checks and balances, environmental upsets associated with newly arrived or rare organisms are uncommon.

However, these ecological upsets do occur. They take place under two circumstances. First, when the natural system of checks and balances is disturbed. This system of checks and balances can be perturbed, and much attention has been given to the reasons.

Second, when species not previously present in an environment are introduced into that environment. The establishment of the so-called exotic species is known to have occurred for sparrows and many other birds, the rat and mongoose among mammals, the gypsy moth and many other types of insects, a host of plant species that are commonly called weeds, and microorganisms that cause major diseases of agricultural crops, trees, animals, and even of humans.

Although one might question the applicability to genetic engineering of our knowledge of the harm done by exotic species, that information is much more useful than untested and often unconvincing hypotheses about the lack of establishment or effect of an organism whose behavior in nature is totally unknown.

Ecologists are embarrassed to admit that they cannot predict whether a currently existing species will or will not become established when introduced into a new environment. If ecologists cannot make accurate predictions for existing organisms in a problem area that is ecological, how can a nonecologist make a convincing statement about a newly modified organism, one for which there is no environmental experience?

What should we know in order to reduce the level of uncertainty arising from the planned, deliberate release of engineered organisms? Five areas of ignorance stand out.

First, will the engineered organism survive? Obviously if it does not survive, it will pose no hazard. But likewise, a nonsurvivor would be of little practical interest to industry because it would have little market value.

Second, will the organism multiply? For many species, the few individuals that endure do not constitute a problem in agriculture, ecology or public health, but should they multiply and reach large populations, major disturbances become evident.

Third, is the potentially deleterious genetic information transferred from the deliberately released organism to other species? The organism that is released may not endure, but those traits that serve as the bases for concern might be passed to another organism in the same environment.

Fourth, is the engineered organism transported or disseminated to new sites? Many microorganisms and plants fail to be transported for any distance, but other species are widely dispersed and soon appear at considerable distances from the point of their first introduction. Witness at the moment the organism causing citrus canker, which is not engineered, but it is suddenly appearing where we could not predict.

Fifth, will the introduced organism have a deleterious effect? This, of course, is the critical question. It is my belief that most genetically engineered organisms will not pose problems because

most will not survive, most that survive will not multiply, gene transfer is reasonably infrequent, most that survive and multiply will not be transported to a distant place, or most transported organisms will not have the traits needed to cause injury. The fact that most engineered organisms will fail one of these tests does not mean that all will. Which organisms will fail one or more of these environmental tests cannot now be predicted.

Indeed, our knowledge is so limited that it is not even possible to state the characteristics that result in failure or success. Large uncertainties exist in anticipating the environmental consequences of genetic engineering because of these major knowledge gaps, gaps in the subjects of survival, multiplication, gene transfer and dissemination.

Can we even predict the potential of novel organisms for doing harm? The information on ecological upsets and on diseases of plants, animals and humans is abundant. Enormous numbers of human deaths have resulted from the introduction of microorganisms into regions where the people were not previously exposed to the harmful agent, and the decimation of the population of Indians in North and South America and of the original inhabitants of the Pacific islands bears witness to the susceptibility of previously unexposed populations. The responsible microorganisms were not deliberately modified genetically, but simple genetic changes that have occurred and do still occur in nature have been the prelude to major human diseases. These genetic changes may not be too different from those that are currently of interest in genetic engineering.

In addition, agricultural crops have often been devastated following the introduction of a new disease agent, and many of these disease-producing microorganisms are genetically very similar to species that previously had little effect.

As I have said, it is my belief that the probabilities of survival, multiplication, gene transfer, dispersal and detrimental effects are quite small and, therefore, the probability of the final event in the sequence is even smaller. Nevertheless, I do not know how small is a small probability.

Moreover, as genetic engineering uses new techniques, is applied to more organisms and is more widely used, an event that may take place one time in a thousand will occur because the type of event has been repeated 1,000 times.

Let me stress what I believe is a crucial point: In the absence of a substantive body of scientific information to allow for reliable predictions, and in the absence of data from tests designed to provide information on individual genetically engineered organisms, it is utterly foolhardy to anticipate what may or may not happen in nature.

Scientists notwithstanding, uncertainties will remain even as we gain more information, but at least the degree of uncertainty and presumably the likelihood of a problem arising will be substantially reduced as the information is obtained.

The degree of uncertainty can also be reduced by data from appropriate tests mandated by a regulatory agency. Even with a wealth of scientific data, testing is important because science provides generalizations, guidelines and approaches, but exceptions to

the rule are not exceptional. Science can reduce but surely not eliminate the uncertainty. Hence, it is essential that a regulatory agency require a meaningful but not onerous series of tests to evaluate potential hazards.

I am excited by the prospects and benefits of genetic engineering. I am also impressed by how little we know of the potential behavior of deliberately introduced organisms. I believe that the considerable uncertainties that remain among environmental scientists can be reduced very markedly. This can be accomplished by research designed to predict the behavior of novel organisms and by regulations that require industry to provide information to allow for assessment of safety or hazard. In this way, I believe that we shall be able to gain the benefits of an extremely important new technology while minimizing the risk to humans, agriculture and our environment.

Thank you.

Senator DURENBERGER. Thank you very much.

Dr. Brill.

STATEMENT OF DR. WINSTON BRILL, VICE PRESIDENT, RESEARCH AND DEVELOPMENT, AGRACETUS CORP.

Dr. BRILL. If there is one message I leave with you today, it is that there is no reason to believe that use of a genetically engineered plant, bacterium or fungus to be created in the foreseeable future will in any way be any less safe than those agricultural practices and products in common and widespread use in the world today. This conclusion is based on our actual experience as a society with current and historical agricultural practices. This conclusion is supported in detail in my written testimony, but I think it is helpful if I emphasize its most important points here.

This is midwestern corn. To make this plant even more valuable, corn breeders continually look for new gene sources and try to make valuable hybrids between this plant and others. These breeding practices over many decades have had a major positive impact on U.S. agriculture.

This is teosinte, a Central American wild grass which is now presumed to be the ancestor of our modern corn. Scientists around the world have been crossbreeding corn lines with teosinte in order to introduce new genes into corn; for instance, to achieve better disease resistance in corn.

Thousands of such hybrid crosses are performed in fields in this country and others. When these two plants are crossbred, they mix all of their hundreds of thousands of genes randomly to yield progeny with a wide spectrum of genetic characteristics. These crossbreedings would not occur without man's intervention, and the characteristics of these progeny are impossible to predict even for those most skilled in plant genetics.

Thus, under commonly used genetic practices, we are adding hundreds of thousands of unknown genes into our common commercial crop plants through traditional agricultural practices. In comparison, the new genetic engineering technology will add a few characterized genes to a plant. The properties of the progeny from a genetic engineering experiment will be far easier to predict than

those produced through a cross between corn and teosinte. That is design. That is engineering. That is genetic engineering.

Senator DURENBERGER. When are you bringing on the cow?

Dr. BRILL. Breeders are not concerned that any plant resulting from such a cross between corn and teosinte will spread in an uncontrolled manner; in other words, become a problem weed. This is in spite of the fact that new, entirely uncharacterized genes are being introduced into the corn plants. The lack of concern is based on the many centuries of experience mankind has had as a plant breeder.

Corn seed, if thrown into your yard or into the woods, will not take over like dandelions or crab grass would. Scientists now understand that at least hundreds, and perhaps thousands, of very specific genes are necessary to convert corn into a problem weed. It is not reasonable to expect that in the foreseeable future any laboratory could hope to purposely engineer corn to become a problem weed. To do so by accident is essentially impossible.

Thus, in the genetic engineering of plants, where one or several well-characterized genes are intentionally put into specific domesticated plants, the possibility of any plant coming out of this process which could in any way be a competitive weed is even more unlikely.

The prospect of genetic engineering of plants offers the possibility of reducing some of the adverse genetic consequences of present agricultural practices. Current practices with chemical herbicides and insecticides frequently cause genetic changes in weeds and insects. In other words, we are now causing gene changes in dangerous organisms.

It is paradoxical that it is the very goal of many of the genetic engineers to make our future agricultural practices less dependent on such chemicals with their adverse consequences. Let me stress this: Most applied genetic engineering work currently going on is aimed to replace some of our most noxious chemicals. As an environmentalist, I am happy to be involved in this activity.

It has been said that because we struggle now with several problem organisms, such as kudzu vine, Japanese beetle, or gypsy moth, that we need to have concerns about genetically engineered plants. This assertion is faulty in its premise. These problem organisms are not the result of relatively minor genetic changes, such as those the genetic engineer would make. When kudzu, Japanese beetle and gypsy moths came to the United States, they thrived because their natural competitors were lacking and, therefore, the introduced organism took over in their new environment. That is why kudzu vine, Japanese beetle, and the gypsy moth have caused problems.

It is the purpose of our laws governing importation of organisms from other countries to help us control these kinds of problems. There is nothing about these experiences that would suggest that any plant, with changes, additions or deletions of one or a few characterized genes could create this kind of problem.

The point I am making here is equally applicable to microorganisms, such as bacteria and fungi, for agricultural use, as it is to plants. So let me talk briefly about microorganisms.

Here is a container filled with bacteria that was once sold to improve the growth of clover. On the label on the box it says that it contains 15 billion germs, for 1 bushel. This was produced in 1920. I am showing it to you to illustrate that bacteria and fungi have been freely grown in huge quantities for many decades and that field experiments have been conducted around the world using these organisms. Such introduced organisms in the soil continually mutate and exchange genes, resulting in a great genetic variability of the organisms we added.

Each year new microbial products for agricultural use are introduced. Yet in spite of all of this widespread use, there has never been a single confirmed report that I know of in which a microbial culture, considered safe, has caused a significant problem in any field, even in its experimental field testing stages.

As a society we constantly add cultures of microorganisms to our environment. Cultures of billions of uncharacterized microbes are added to the environment every time a piece of rotted fruit or other food is thrown into the woods. Environmentalists are not concerned that the ecology of those woods will be disrupted. There are reasons why there has been no such problem. Nature is resilient, and the original balance of microbes tends to return to an environment over time. There is no reason to believe that a microbe which does not now cause problems to the environment will persist in the environment or begin to cause problems when it has a few well-characterized foreign genes added to it.

You may ask what is the chance that we could accidentally produce a disease-forming microbe by genetically engineering, for agricultural use, a known harmless microbe. Scientists have now shown us that many genes are necessary for an organism to become a problem pathogen. Thus, the chance of accidentally creating a microbial pathogen by introducing a few identified genes in a nonpathogenic microorganism is virtually nil.

It would perhaps be more settling to the public at large if laboratory or greenhouse tests could demonstrate that a particular genetically engineered plant or microbe would be safe in the general environment. However, there is no way known to mimic the complex interactions between plants, microbes, soils, soil treatments, and the weather. In order to test the effect of any agricultural product, field tests are essential.

In summary, from practical and scientific experience, I assert that it would be extremely difficult to purposely engineer a plant, bacterium or fungus now considered harmless to become a significant problem to the environment or to public health. To make a harmless organism become a problem accidentally while creating an organism useful to agriculture is virtually impossible.

The very improbable risk scenarios described by the opponents of this technology obviously need to be weighed in balance with the benefit to be obtained from it. As Thomas Jefferson once said, "The greatest service which can be rendered any country is to add a useful plant to its culture."

My message today is that I do not see any likelihood of any potential serious negative environmental consequences of genetic engineering of agricultural plants or microorganisms in the foreseeable future. Therefore, I do not believe there is any need to rush

into any overhaul of the existing review and regulatory procedures, which we believe are adequate, since the possibility of harm is so small and the probability of benefit is so great.

Of course, we are hurting personally, but I mention this because we are contending for the lead in the United States and, hopefully, the United States will be the world leader in agricultural applications of genetic engineering. Agracetus has lost two growing seasons, 2 years, because approval from NIH has still not been granted, even though the Recombinant DNA Advisory Committee has twice approved, on the basis of an extensive review of safety considerations, Agracetus' request to perform a very small and contained field test.

Thank you.

Senator DURENBERGER. Thank you very much.

On that latter point, would you explain why you can't just go ahead with the field test?

Dr. BRILL. We are waiting for Dr. Wyngaarden's OK which we have not received.

Senator DURENBERGER. Why do you have to wait for them?

Dr. BRILL. Because we want to comply with the NIH RAC guidelines.

Senator DURENBERGER. Why do you want to comply with them?

Dr. BRILL. It is important for us, No. 1, to be perceived as being a responsible company. It is important for me personally to actually be responsible. And it is a new technology, and I think a new technology ought to have at least some kind of review.

Senator DURENBERGER. Other than for those reasons, do you think you have to wait? What seems to be holding it up?

Dr. BRILL. We don't have to wait. We would rather go by whatever regulations the U.S. Government comes up with, if any.

Senator DURENBERGER. Let's talk about that, Dr. Alexander. Would you describe for us the kinds of tests that you think would be needed in a regulatory program for release of novel organisms?

Dr. ALEXANDER. I think it is not too difficult to do most of the types of tests that are required. They are not difficult. They will not be expensive. The items in the areas of ignorance I indicated would reflect the sorts of tests. Will the organisms survive? It is simple to measure. Will the organism multiply? That, too, is simple to measure. Will it transfer genetic information? That could be a real problem to test. Is it transported from place to place? That, too, one can measure.

The difficult area where I think there needs to be research is in the area of measuring effects. That we do not know how to do in a convenient, testable system.

Differing from what Winston Brill said, I do believe there are systems that EPA has developed for testing reasonable environmental models so that we can measure interactions among species in a contained area.

These tests are simple, straightforward, not time consuming and not overly expensive, except for the last procedure, measuring effects. I would expect that most organisms that are being considered for genetic engineering will fail one of those four tests, so that they will be approved.

If an organism passes all four and has to be tested for its impact on plants and animals, it will take time and it will be expensive. But I think it is a degree of caution we ought to have in order to protect ourselves.

Senator DURENBERGER. Dr. Brill, do you want to react to that?

Dr. BRILL. Yes. If there are tests that are relevant, I would certainly very much support them. I am a bacteriologist. The first test I guess was just to look at populations in the field. Depending on the organism, and I would predict it would be for most organisms that would be used in the future, that can be extremely difficult and would involve, in fact, more genetic engineering to get markers so you can pick out the one organism of the millions that are in a handful of soil.

For some organisms there are simple ways to examine populations in the field. For most microbes, I think most that will be applied to agriculture, there are no ways of doing it. It may not even be relevant to determine population levels. In other words, in some situations one organism per handful could be a problem, and in other cases a billion organisms per handful might be needed to cause a problem.

In some disease cases, a couple of organisms can cause illness. In other cases many, many, many are needed to cause disease. So, I question the relevance of the data. I mean one can do experiments, but thought is required to determine the relevance of the results to safety questions.

This is probably the best understood microorganism that is used in agriculture today. It is called Rhizobium. Today, with the laboratory work of Martin Alexander and myself, Winston Brill, and hundreds of other laboratories over many, many decades, I can't tell you very easily if I threw this in the soil how long it will persist, or how well it would increase in number in the field. It is extremely difficult.

Now, this organism is among the best understood of bacteria. Other organisms are not so well understood.

Senator DURENBERGER. Dr. Alexander, in your statement you said that many of the microorganisms that have devastated our crops are genetically similar to the species that previously had little effect. Are you saying that even minor changes in the genetic make-up of an organism can lead to what you might call major differences in effects on plants and animals?

Dr. ALEXANDER. I can cite worst case examples where the answer is yes. There are a number of instances where a simple genetic change alters an organism from a harmful species to a nonharmful species, and presumably the other can be done as well, and in some cases it has been shown. In fact, one of the pioneering experiments in the field of molecular genetics did essentially that.

My concern isn't that I think it is simple to make these changes. The concern is that I am not sure. There are examples of potential problems with these genetic changes. There are many, many examples of nonproblems. This is why, given the expanding scope of the technology, I think we do have to have the information. We do have to have the tests for specific species.

Senator DURENBERGER. Are you saying that a gene that is deliberately placed in one organism can be transferred to a different kind of organism?

Dr. ALEXANDER. The gene can be transferred to different organisms, that is correct, or the genetic make-up of a single organism can be modified so it will affect a plant or an animal. We have good examples in human pathology—pneumonia, for example. Or we can potentially change an organism so it acts on different species. That is the issue underlying the need for regulation of microorganisms to be used as pesticides.

Senator DURENBERGER. Obviously, in the agriculture field we are worried about placing a gene in a controllable organism, like a corn plant, which might get transferred to a weed, for example. What kinds of environmental consequences occur from that kind of a transfer?

Dr. ALEXANDER. I am a bit more familiar with the microorganism side of things. But if a deleterious gene is transferred and is expressed, then the potential for a problem does exist.

We have very few examples of which I am aware in the field of plant sciences. However, the potential is there. As we move away from simple recombinant DNA technology to a variety of genetically more complex manipulations, the probability of this event goes from, let us say, vanishingly small to reasonably small.

Senator DURENBERGER. Why don't you take a crack at that question with regard to microorganisms.

Dr. ALEXANDER. We know that many organisms that do no harm are very similar to organisms that cause considerable injury, as in the current concern with citrus canker. Members of the same group of organisms are widespread in nature but do no harm at all, or act on entirely different plants.

If the genetic information, and in some cases that is a small amount of genetic information, is then transferred to a harmless organism, that new organism could, in fact, do injury.

I think the probability is very small because that should have occurred in nature. But we can do much more genetically in the isolated laboratory than in nature and in a short period of time.

Senator DURENBERGER. Dr. Brill, do you want to respond to that?

Dr. BRILL. I guess I disagree with that last statement. I think nature is much more versatile than any of the genetic engineers that are presently working and those that will be working. People have appreciated the dynamics of gene exchange in nature. There are naturally systems where bacterial genes, without man's intervention, have gotten into plants, If two organisms are somewhat related, you can bet they will exchange genes, in every single combination. So there is tremendous versatility.

The one thing I would like to comment on is Dr. Alexander's statement that problems have been caused by certain gene changes in nature. That is true. I mentioned a couple. I mentioned insect resistance to insecticides and weed resistance to herbicides. You can take microbes that are resistant to antibiotics.

Those became problems not because of gene change. Those became problems because of man's addition of chemicals. All of these problems can be remedied merely by removing the chemicals.

He is absolutely right, it is a one-gene change. But it is not that all of a sudden something came up and we are straddled with a problem. What came up was the chemical selection which forced that gene to change. That is very, very different than what we are talking about regarding genetic engineering.

Senator DURENBERGER. On Thursday, Dr. Daniel Simberloff, who is an expert on invasion by exotic organisms, may differ with that statement. I think he is going to indicate, and he uses the apple maggot, the planthopper, and maybe some others as examples, that there is a spontaneous change involved in these kinds of invasions or outbreaks or whatever. Would you disagree with that?

Dr. BRILL. No; I agree with that. In fact, Dr. Alexander said problems frequently occur when you change the ecology, change the environment somewhat. One way to change the environment is to bring in a new plant. Sometimes when you bring in that new plant you may also bring in an insect that doesn't like living, let's say, in the United States that much, but eventually there will be a mutation where the insect does well in its new environment and causes problems.

Senator DURENBERGER. Dr. MacLachlan, let me ask you: Suppose we have a frustrated bacteriologist who is associated with an effort that might make the United States of America the world leader in a certain area but can't get approval to test his product through a Federal organization that doesn't want some of this regulatory responsibility. Obviously, if duPont is known for anything, it is known for innovation and it is known for leadership in a wide variety of areas and for making this country a leader in a lot of these areas.

Where are we left here in the near term in balancing regulation against experimentation and innovation? How far do we have to go in the direction that Dr. Alexander recommends we go, that we go to the testing of genetically engineered organisms so that we don't get in the way, if you will, of some process of new product development and innovation?

Dr. MACLACHLAN. I guess I look at it like this. We are in the early stages of a learning curve. As you said, Senator, in your introduction, this is an embryonic science and there is a lot to be learned as we progress with its implementation into commercial products. In my opinion, this is natural. There are a lot of things we now are worried over and not sure about. However, as we progress together on the learning curve we will be able to convince the public we are responsible and are proceeding with due regard for safety.

How do we do this? I guess I look at it as a partnership made up of industry, the appropriate Government agencies, and scientific experts. The existing agencies like the FDA and so forth have had long experience in effectively dealing with conventional materials, but now they are faced with dealing with these bioltechnology produced materials. While in many cases, this is not really dealing with anything fundamentally different, especially as far as the desired effects go, there are many new considerations to manage.

It seems to me, even though I am not a bacteriologist or biologist, the risks are extremely low and I think Dr. Alexander has said that. It also seems to me that we must, for the time being, evaluate

each situation on a case-by-case basis. As I just said, industry working with the appropriate Federal agency and in turn working with scientists skilled in the new technology is the way to do it. Right now the best skill group already in place is the RAC, and they should continue to be used.

I would hope we can start right now with this partnership and maintain it through the infancy of this new industry. I don't know any other way to do it. We need to listen to the concerns and address them. Sometimes this may force us to slow down or cost substantial sums of money. In most cases I think we can expeditiously resolve the concerns at least to a point of minimum risk. We will, of course, ultimately have to take some risks. However, for the most part, the kinds of questions we will be dealing with in the near future will not be that complex or costly to satisfy relative to our concerns.

As we progress with this new technology, we will be dealing with ever more complex questions, but we will also have more knowledge and experience. For example, moving several genes around simultaneously. Where today that might present some very hard questions to answer, in the future we will feel comfortable with such advanced technology. So let's go forward with a partnership.

Senator DURENBERGER. Dr. Alexander, following on that same line, I wonder what your views might be about regulation in this area in the general sense. Clearly if we enlarge the scope of the environmental problem and I don't know anything about Dr. Brill's specific request that he has before NIH, but if we enlarge the scope of the perceived problem, then it seems to me we delay the time at which we can address certain kinds of products, if you will, that don't present quite that large a problem, maybe a lesser problem.

I don't know whether Dr. Brill is caught in that kind of situation or not. But I think we all understand that regulation in this area of the environment is undergoing some change and that if we rely on existing bureaucracies, whether it is NIH or EPA or the FIFRA people at USDA or whatever, they are more likely, under societal pressure, to do nothing or to overreact or, as they say, protect the opinions and the reputations of the bureaucracy. In other words, to slow down the process of decisionmaking rather than to speed it up or encourage it.

I am curious to know whether or not after you have told us here in a very practical sense some of the knowledge base we need to fill whether you have some suggestions about the process for filling them. Dr. MacLachlan gave us some specific recommendations on the regulatory approach. Do you have some specific recommendations to make to us as you look at the role that TSCA plays and some of these other Federal laws?

Dr. ALEXANDER. If we have a high-risk technology, as we have in the case of pesticides or drugs, then obviously one must have an expensive and very careful evaluation. I think we all agree that this is a low-risk technology, but I don't agree it is a no-risk technology.

If that is the case, I think we do have precedents in the Federal system for regulations of new materials that are being introduced. TSCA has that concern under Section 5, the PMN procedure. That approach requires no information for the PMN. The information

has to be provided if it is available, but it requires developing no new information.

This approach, I think, would have to be modified because in the field of behavior of novel organisms, in contrast with the behavior of novel chemicals, we don't yet have a science. I think that some modest information ought to be required.

As you know far, far better than I do, speeding up the bureaucracy is not easy to do. The process will be slow. The testing will impose a cost. It will delay industry. But if the precedent of TSCA and the PMN system were a bit more concerned with novelty and with biology than presently exists, and if this is coupled with some science, we would have a reasonable degree of certainty, a minimum of delay prior to the development of products and a maximum of benefit for agriculture and in pollution control.

So I do not believe that we are really proposing anything that enormous in terms of a regulatory system. I believe it can be done. But the two things that are really required are a sensible regulatory framework and information which does not not exist in this area.

Senator DURENBERGER. Dr. Brill, now that you have had considerable experience with our current approach and you have heard from EPA here earlier today about some of the areas in which they propose, through the rulemaking process, to get involved in, what are your recommendations as to how we might structure this regulatory response?

Dr. BRILL. I guess my first recommendation is that somehow the danger/safety issues that have been mentioned here ought to be discussed at a scientific level.

After that, or after the results of such discussions have been reviewed, if the public still has a concern, there ought to be some type of regulation and, hopefully, that regulation will be based on scientific experience and the public's knowledgeable perception of the safety issues.

Senator DURENBERGER. Dr. Alexander, you heard me refer in my opening statement to lignin, because it is my understanding that scientists are experimenting on the effect of the decomposition of lignin and perhaps how it affects other fundamental functions of the ecosystem. Do these kinds of experiments trouble you? In other words, are there some kinds of genetic manipulations that in your opinion are more environmentally dangerous than others that we can predict?

Dr. ALEXANDER. There are a number of visible munipulations. The lignin case is a good point. Steps in the process we know as nitrification represent another case. In each instance, let's say I am quite concerned about this. I would like to have meaningful environmental information, and I would like to have good tests, and not simply than a group of people who merely vote for what is good or is bad without having data from tests and from research.

I probably am wrong in my concern with these processes, and other people can come up with better scenarios for ecological perturbations resulting from some type of genetic manipulation. It is when these legitimate concerns are laid to rest, using data from research or testing, that I think we would feel much more comfortable. As we know, even in the area of drugs, there will be products

that slip by our research and testing guidance. Thalidomide is a good example of this. But the frequency of problems is markedly reduced once there is good scientific information once there is good regulation.

Senator DURENBERGER. Do either of the others want to comment on the question of whether or not there are certain genetic manipulations that are clearly more environmentally dangerous than others? Dr. Brill?

Dr. BRILL. I would like to comment, since you introduced the session with the lignin problem, that a lot is known about lignin degradation. Organisms that are best at degrading lignin do so very, very slowly. People are studying how lignin is degraded. Lignin is an extraordinarily complex molecule. Many, many enzymes are required in order to degrade lignin. Once again, the chance of doing so accidentally is nil. I mean if one wants to do so purposely, it would take at this point I think a number of years of research focused on lignin degradation to get an organism unable to degrade lignin to be able to do so efficiently. That is, to get it to degrade lignin at rates equivalent to those in organisms already in our environment.

Another point I would like to make, which I think is important, is your frequent comparison between regulation of chemical products and biological products. If a chemical is known to be safe, a minor change in its structure may make it exceedingly dangerous. Because of this, the new chemical has to be tested independently of the knowledge that the first chemical is safe. That is not true for microorganisms. Microorganisms or plants or animals have consistently been very variable, with the differences in cattle, differences in plants, the differences in microbes. So we have gotten to live with variability and feel safe with it. I think you have to be careful when you compare chemicals with organisms.

Senator DURENBERGER. Thank you all very much. We certainly do appreciate the time and effort that you have put into your testimony today.

The hearing will be adjourned. We will reconvene on Thursday morning with the second half of our hearing.

[Whereupon, at 12:05 p.m., the subcommittee was recessed to reconvene at 10 a.m. Thursday, September 27, 1984.]

[Statements submitted for the record follow:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20205

STATEMENT

BY

BERNARD TALBOT, M.D., PH.D.

ACTING DIRECTOR

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

NATIONAL INSTITUTES OF HEALTH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS

SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT

UNITED STATES SENATE

SEPTEMBER 25, 1984

I am Dr. Bernard Talbot, Acting Director of the National Institute of Allergy and Infectious Diseases, at the National Institutes of Health. I have been associated, since 1975, with the original preparation, and with all subsequent revisions, of the NIH Guidelines for Research Involving Recombinant DNA Molecules. These safety standards were developed in response to a request by scientists[1] that the National Institutes of Health devise "guidelines to be followed by investigators working with potentially hazardous recombinant DNA molecules."

Overseeing the NIH Guidelines is the NIH Recombinant DNA Advisory Committee (called RAC for short). The RAC consists of 25 voting members appointed by the Secretary of Health and Human Services, plus non-voting representatives of Federal agencies[2] who participate actively in the RAC meetings. The voting members include eminent scientists of many different disciplines, a lawyer, a former State legislator, an occupational safety expert, a housewife, practicing physicians, and a bioethicist. Federal agencies with representatives on the RAC are the: National Science Foundation; Department of Agriculture; Environmental Protection Agency; Food and Drug Administration; Department of State; Veterans Administration; Department of Energy; Centers for Disease Control; National Institute for Occupational Safety and Health; Department of Commerce; Department of Interior; Department of Transportation; National Aeronautics and Space Administration; Department of Labor; Department of Defense; and Office of Science and Technology Policy.

Any proposed revision of the NIH Guidelines must first be published for public comment, and then discussed and voted on by the RAC in open session, before it may be adopted by NIH.

The NIH Guidelines were first issued in July 1976.[3] Those 1976 Guidelines included classes of experiments that were "not to be performed." This included "deliberate release into the environment of any organism containing a recombinant DNA molecule."

The first revision of the NIH Guidelines, issued in December 1978[4] reorganized the classes of experiments previously listed as "not to be performed" into a section entitled "Prohibitions" including "deliberate release into the environment of any organism containing recombinant DNA." However, the Guidelines noted that "Experiments in these categories may be excepted from the prohibitions . . . provided that these experiments are expressly approved by the Director, NIH, with advice of the Recombinant DNA Advisory Committee after appropriate notice and opportunity for public comment."

The revision of the Guidelines issued in April 1982[5] changed the section entitled "Prohibitions" to one entitled "Experiments that Require RAC Review and NIH and Institutional Biosafety Committee Approval Before Initiation." Included again under this category was "deliberate release into the environment of any organism containing recombinant DNA."

The most recent complete revision of the Guidelines, issued in June 1983[6] specifies new procedures to facilitate the approval of field

testing under certain specified conditions of certain plants modified by recombinant DNA techniques; these now require review by the RAC Plant Working Group, but no longer by the full RAC, prior to approval by NIH.

In addition to review by the full RAC, or the RAC Plant Working Group, prior to approval by the NIH, any deliberate release to the environment also requires prior approval by the local institutional biosafety committee.

To date three cases of deliberate release to the environment have been approved by NIH. In each such case:

(1) Notice was placed in the Federal Register at least 30 days prior to the RAC meeting at which the proposal was discussed, giving notice and inviting public comment on the proposal.

(2) The proposal was discussed at an open session of a RAC meeting, with active participation in the discussion by the Department of Agriculture representative. During the discussion the RAC carefully considered the possible hazards of the experiment. This involved some RAC members proposing "scenarios" of possible hazard, and other RAC members replying as to why the "scenarios" were extremely unlikely to occur. Following the discussion, the RAC voted in each of the three cases to recommend approval of the proposal.

(3) Advice was sought from the Department of Agriculture Recombinant DNA Advisory Committee which in each of the three cases recommended approval of the proposal.

(4) NIH approved each of the proposals with a notice in the Federal Register explaining the request, and the reasons for granting approval.

The three cases are: approval to Dr. Ronald Davis of Stanford University[7] to field test corn plants transformed by corn DNA; approval to Dr. John Sanford of Cornell University[8] to field test tomato and tobacco plants transformed with bacterial and yeast DNA; and approval to Drs. Steven Lindow and Nickolas Panopoulos of the University of California, Berkeley[9] to release Pseudomonas syringae and Erwinia herbicola carrying deletions in the genes involved in ice nucleation, for purposes of biological control of frost damage in plants. None of these field tests has actually been conducted to date.

NIH is not a regulatory agency and has no statutory authority over industry. NIH's mission is the funding of research, and it has authority to impose requirements only on those institutions which accept NIH research funds, with the maximal possible penalty for non-compliance being the cutoff of such NIH funds. Most of industry does not receive NIH funds for recombinant DNA research, and, therefore, is not required to comply with the NIH Guidelines.

During the 95th Congress (1977-1978) sixteen different bills dealing with recombinant DNA were introduced. The most extensive set of hearings[10] were held by the House Subcommittee on Science, Research and Technology, chaired at that time by Congressman Ray Thornton. (After leaving Congress, Mr. Thornton subsequently was a member (1979-1982) and Chairman (1980-1982) of the NIH Recombinant DNA Advisory Committee). In the Senate hearings were held both by the Subcommittee on Health and Scientific Research, of the Committee on Human Resources, and by the Subcommittee on Science, Technology and Space, of the Committee on Commerce, Science and Transportation. Bills which would have made the NIH Guidelines mandatory for the entire country passed Committees in both the House and Senate but never reached the floor of the House or Senate for a vote. There is therefore today no national law making the NIH Guidelines mandatory for private industry.

In the absence of national legislation, New York State and a number of localities[11] have passed local legislation making the NIH Guidelines mandatory. For the rest of the country other than these localities, for work not supported by Federal funds, compliance with the NIH Guidelines is not mandatory. There is, however, a section of the NIH Guidelines entitled "Voluntary Compliance" which encourages commercial organizations to comply voluntarily with the Guidelines. At the last RAC meeting on June 1, 1984, two proposals for field tests of genetically engineered organisms voluntarily submitted by private companies were reviewed and recommended for approval; a final NIH decision on these proposals has not yet been made.

In September 1983, a law suit[12] was filed by Jeremy Rifkin and others charging violation of the National Environmental Policy Act, and in May 1984 Judge John Sirica issued a preliminary injunction enjoining the NIH from approving "deliberate release" experiments submitted by NIH grantee institutions, although specifically allowing NIH to approve such experiments voluntarily submitted by industry. The government is appealing the preliminary injunction.

In April 1984 the Cabinet Council on Natural Resources and Environment Working Group on Biotechnology was established.[13] It consists of "representatives of the Departments of the Interior, State, Justice, Agriculture, Commerce, Energy, Health and Human Services and Labor, the Environmental Protection Agency, the Council on Environmental Quality, the Council of Economic Advisers, the Office of Management and Budget, the Office of Policy Development, the Office of Science and Technology Policy, and the National Science Foundation." It is directed "to undertake a review of the federal regulatory rules and procedures relating to biotechnology" including reviewing the function of the NIH Recombinant DNA Advisory Committee "and its role in biotechnology commercialization and safety regulation."

This concludes my prepared testimony. I will be pleased to answer any questions.

FOOTNOTES

1. "Potential Biohazards of Recombinant DNA Molecules" appeared simultaneously in Science 185, 303, 1974; Nature 250, 175, 1974, and the Proceedings of the National Academy of Sciences 71, 2593, 1974, by Drs. Paul Berg, David Baltimore, Herbert Boyer, Stanley Cohen, Ronald Davis, David Hogness, Daniel Nathans, Richard Roblin, James Watson, Sherman Weissman and Norton Zinder.

2. The representatives of Federal agencies to the NIH Recombinant DNA Advisory Committee are: Dr. Herman Lewis, National Science Foundation; Dr. Sue Tolin, Department of Agriculture; Dr. Morris Levin, Environmental Protection Agency; Dr. Henry Miller, Food and Drug Administration; Dr. William Walsh, Department of State; Dr. Richard Green, Veterans Administration; Dr. George Duda, Department of Energy; Dr. Walter Dowdle, Centers for Disease Control; Dr. Richard Lemen, National Institute for Occupational Safety and Health; Mr. John Cox, Department of Commerce; Dr. Mariano Pimentel, Department of the Interior; Dr. George Cushmac, Department of Transportation; Dr. Donald DeVincenzi, National Aeronautics and Space Administration; Dr. Ralph Yodaiken, Department of Labor; Dr. William Beisel, Department of Defense; and Dr. Bernadine Bulkley, Office of Science and Technology Policy.

3. NIH Guidelines for Research Involving Recombinant DNA Molecules. Federal Register, July 7, 1976, Part II, pages 27902-27943.

4. NIH Guidelines for Research Involving Recombinant DNA Molecules. Federal Register, December 22, 1978, Parts VI and VII, pages 60080-60131.

5. NIH Guidelines for Research Involving Recombinant DNA Molecules. Federal Register, April 21, 1982, Parts II and III, pages 17166-16198.

6. NIH Guidelines for Research Involving Recombinant DNA Molecules. Federal Register, June 1, 1983, Parts II and III, pages 24548-24581.

7. Approval appeared in the Federal Register, August 7, 1981, page 40331.

8. Approval appeared in the Federal Register, April 15, 1983, page 16459.

9. Approval appeared in the Federal Register, June 1, 1983, page 24549.

10. Hearings before the Subcommittee on Science, Research and Technology, Committee on Science and Technology, U.S. House of Representatives, on "Science Policy Implications of DNA Recombinant Molecule Research." Hearings held on March 29, 30, 31; April 27, 28; May 3, 4, 5, 25, 26; and September 7 and 8, 1977.

11. Localities requiring compliance with the NIH Guidelines are: Amherst, Massachusetts; Berkeley, California; Boston, Massachusetts;

Cambridge, Massachusetts; Emeryville, California; Newton, Massachusetts; Princeton, New Jersey; Somerville, Massachusetts; and Waltham, Massachusetts.

12. Foundation on Economic Trends, et al., v. Margaret M. Heckler, et al., Civil Action No. 83-2714 in the United States District Court for the District of Columbia.

13. Memorandum of April 30, 1984 from Martin L. Smith, Deputy Assistant Director for Energy and Natural Resources, Office of Policy Development, the White House, to the Secretary of the Interior; the Secretary of State; the Attorney General; the Secretary of Agriculture; the Secretary of Commerce; the Secretary of Energy; the Secretary of Health and Human Services; the Secretary of Labor; the Administrator, Environmental Protection Agency; the Chairman, Council of Environmental Quality; the Chairman, Council of Economic Advisers; the Director, Office of Management and Budget; the Director, Office of Science and Technology Policy; the Director, Office of Policy Development; and the Director, National Science Foundation.

STATEMENT OF
DR. JOHN A. MOORE
ASSISTANT ADMINISTRATOR
FOR PESTICIDES
AND TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS
SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT
UNITED STATES SENATE

SEPTEMBER 25, 1984

Mr. Chairman and members of the Subcommittee, I am Dr. John A. Moore, Assistant Administrator for EPA's Office of Pesticides and and Toxic Substances. I am pleased to have this opportunity to discuss with the Subcommittee this morning the future directions the Environmental Protection Agency (EPA) is considering in the regulation of genetically-engineered organisms. Two offices within EPA, the Office of Pesticides and Toxic Substances (OPTS) and the Office of Research and Development (ORD), have been looking at the issue of intentional release of genetically-engineered organisms, and have been developing regulatory programs to address this important issue.

Before discussing the specific actions EPA intends to take in this area, I would like to share with you my perspectives on the growing biotechnology industry. Biotechnology is the application of biological science towards technological ends such as the production or use of chemicals or life forms for commercial or potentially commercial uses. Recent developments in biological sciences have greatly enhanced scientists' ability to manipulate genetic material

and to develop new microorganisms, plants and animals. These advances are expected to lead to the availability of a variety of useful products in a wide range of industries, including chemical production, agriculture and environmental protection. Commercial products of biotechnology are expected to be available in the very near future. The many possible applications of biotechnology may fulfill many of society's needs by alleviating problems of disease and pollution, and increasing the supply of food, energy and raw materials. As with any new process, there are questions about the human health and environmental implications of developing and using microorganisms for commercial purposes, particularly when their use involves a release into the environment. Novel microorganisms, whether they are non-indigenous or whether they are actually genetically manipulated organisms, may be placed in ecosystems where they have not existed before and where natural mechanisms for controlling their populations may not exist.

To address these concerns, EPA is developing a regulatory framework for reviewing certain commercial products of biotechnology that would come under our jurisdiction and review before they are intentionally released into the environment. We will be invoking our statutory authority to review, and where necessary, regulate products intended for commercial use. We are not intending to arbitrarily extend our authority

to all products or processes of biotechnology. Within the next few months, EPA intends to publish two Federal Register notices addressing EPA's statutory authority and planned regulatory approaches in this area. It is my understanding that other agencies that have regulatory authority in this field are also preparing such guidelines.

The first Federal Register notice will be an interim policy statement specifically dealing with the field testing of novel microbial pesticides which EPA is addressing under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). EPA defines novel microbial pesticides to be those which contain naturally occurring microorganisms for use in environments where they are not native, or microorganisms which have been genetically altered or manipulated by humans. This interim policy will require a notification to EPA prior to all small-scale field tests involving deliberate release into the environment. This notification requirement will permit EPA to determine whether an experimental use permit will be required before small-scale field testing is conducted. This interim procedure will not apply to studies conducted in contained experimental facilities such as laboratories, growth chambers, green houses or other facilities where there is no deliberate release of the microbial pesticide into the environment. We recognize that care must be taken

to enable the risk assessment experiments to be conducted in order to build a scientific basis for appropriate regulation. EPA believes that this notification procedure, which will be designed to be timely and efficient, will allow the Agency to evaluate the potential risks of field tests with only a minimum impact on the development of beneficial novel microbial pesticides for use in the environment.

The second and more general Federal Register notice will discuss the Agency's broad policy regarding the regulation of novel microbial products under both the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). This notice will clarify EPA's regulatory authority over novel microbial pesticides and will outline the Agency's specific plans for reviewing and registering these pesticides under FIFRA. The notice will also discuss EPA's proposed policy for reviewing novel microbial products under TSCA. In particular, EPA believes that novel microbial products produced by recombinant-DNA, cell fusion, or other techniques of genetic engineering are "new" chemical substances subject to the Pre-manufacture Notification (PMN) requirements, unless they are substances such as drugs or pesticides that are excluded by statute from TSCA regulation. The Agency also intends to address the applicability of TSCA requirements to field tests or other research and development activities. The notice will provide an opportunity for public comment on how

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the Agency should apply these two statutes to novel microbial organisms. Although a large volume of comments is anticipated, EPA will expeditiously review these comments and promulgate the final policy quickly.

In addition to these activities, EPA's Office of Research and Development is conducting important research in the area of biotechnology to address three important issues: 1) the possible public health and environmental consequences of the release of novel microorganisms into the open environment; 2) the possible public health and environmental consequences associated with the increase of wastes and emissions from a growing biotechnology industry; and 3) the application of biotechnology to improve the environment by degrading persistent and toxic material to provide previously unavailable tools for monitoring pollutants. ORD has already sponsored workshops of scientific experts in this area from academia, industry and government to identify the major areas where knowledge is lacking and to define further the Agency's research plan to address these issues. The consensus of the experts at these workshops noted that considerable information already exists which is relevant to the assessment of microbials including genetically-engineered microorganisms. However, there were recommendations that this information needs further review and should be built upon in the future

to address information gaps and standard protocols that are currently unavailable. Based on recommendations such as these, as well as the technical and regulatory experience from the various EPA program offices, ORD has identified a number of areas where further applied or basic research or other information development efforts are needed. To ensure that the workshop recommendations and EPA plans are appropriately developed, a biotechnology research program management team has been formed to coordinate activities within ORD and to facilitate responses to regulatory office needs.

Obviously, a major issue in any regulation of genetically-engineered organisms is the effect of federal oversight and regulation on innovation in what is a very promising industry. Innovation in the biotechnology field is likely to be of major economic importance to the U.S. economy and to provide significant benefits to the public. Unnecessary or confusing regulations will pose a serious problem to industry and may give a competitive advantage to foreign nations. In addition, the biotechnology field is in its infancy and our regulatory framework must be flexible enough to allow the evolution of policies as new knowledge becomes available. Thus, it is also essential that the federal government coordinate its efforts in regulating this new industry and ensure that any regulations imposed are necessary, consistent, and appropriate.

As the Subcommittee is aware, the Administration has formed an ad hoc working group of the Cabinet Council on Natural Resources and the Environment to address federal regulation in this area and to ensure a consistent overall approach. EPA is an active member of the working group and I serve as EPA's representative. EPA also is working closely with other federal agencies that share an interest in biotechnology including the National Institutes of Health and the Department of Agriculture to coordinate our multiple activities. I believe that a coordinated federal approach in this area involving all interested agencies will permit a highly successful biotechnology industry to exist in this country, while at the same time insuring protection of public health and the environment.

Mr. Chairman, I appreciate the opportunity to provide the Subcommittee with this statement. I will be pleased to answer any questions you may have.

STATEMENT OF

DR. E. L. KENDRICK

CHAIRMAN, USDA RECOMBINANT DNA RESEARCH COMMITTEE

FOR

SCIENCE AND EDUCATION

UNITED STATES DEPARTMENT OF AGRICULTURE

BEFORE THE

SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT

OF THE

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS

UNITED STATES SENATE

SEPTEMBER 25, 1984

Mr. Chairman and Members of the Subcommittee, thank you for the opportunity to testify on the role of the U.S. Department of Agriculture on the subject of this hearing, "The Intentional Release of Genetically Engineered Organisms."

The Department of Agriculture has had responsibility since its founding over a century ago to sponsor research and encourage application of this research for the betterment of the food, feed, and fiber needs of the nation, in both its national and international roles. At its founding the Department was also uniquely enjoined with the Land Grant University development, and as a result the research and application responsibility is fulfilled through state, federal, and private cooperative efforts. We believe this vast network of scientific expertise, laboratories, and controlled environmental facilities, have indeed provided well for the nation in the past, and with our careful planning and introduction of the new biotechnology initiative, including genetic engineering, we will be able to continue to so serve the nation in the future.

I recognize that this Subcommittee's immediate interest is in what is commonly referred to as genetically engineered organisms, and most especially wherein recombinant DNA technologies have been utilized in plant, animal, or microbial species, and deliberate or intentional release of the improved species is desired. However, as background I think it is important to note that the agricultural research community has had a long and highly successful history of developing the genetic components of plant, animal, and microbial life for the benefit of society and its environment broadly.

All the major animal and crop species used for agricultural production in America today have been critically designed and deliberately released. Also, millions of acres of trees are similarly designed to provide part of our fiber needs. In total, these food, feed, and fiber production processes involved deliberate release into the environment of billions of living organisms, each involving design and manipulation of their DNA components. The corn crop alone this year has been estimated to have 193×10^{10} plants, each with its own designed DNA components. Not only did the total agricultural mass of living organisms interact with existing organisms in the environment, it also withstood an array of natural and man-made threats, while contributing vastly to society's well being. Its complexity is staggering.

Recombinant DNA, and other closely related genetic engineering policy issues, are addressed by the USDA Recombinant DNA Research Committee (ARRC). Research in laboratories and other controlled environments, as well as release into the environment broadly is critically assessed. Each agency in the Department that is directly concerned with recombinant DNA research and its application and regulation is represented on the ARRC. In addition the director of the Office of Recombinant DNA Activities of NIH, which administers the Recombinant DNA Advisory Committee (RAC) and the guidelines, is a member of ARRC. Similarly, a National Science Foundation representative is also a member of the committee.

Other research policy committees concerned with recombinant DNA and the new biotechnology in agriculture include the Experiment Station Committee on Organization and Policy (ESCOP), and the Committee on Biotechnology of the National Association of State Universities and Land Grant Colleges (NASULGC).

In the evaluation and review of research involving recombinant DNA, including field experiments, the Institutional Biosafety Committees (IBC's) are an essential feature. This is so both in federal, state, private, and industrial facilities. The IBC's are an essential feature of the RAC and guideline processes.

At the earliest stages of development of RAC and the guidelines for conducting recombinant DNA research, USDA scientists and scientists from the agricultural research community broadly were involved. Along with the scientific community we have strongly supported the concept of a set of standards and procedures for the conduct of recombinant DNA research in the United States. We remain highly supportive of RAC and scientists from the agricultural research community serve on the committee and on special working groups constructed by the committee as needed. The ARRC was designed to be complementary to the RAC processes and is so utilized today. Projects and policy issues involving agricultural interests are reviewed by ARRC on behalf of RAC and in furtherance of the guidelines processes.

In the Department and in the scientific community we find in place mechanisms that provide continual review and oversight of research as new knowledge evolves. These mechanisms also provide for special considerations warranted by genetically engineered organisms.

We highly applaud the RAC process. With a decade of experience we find it has earned wide respect over the nation and the world. Concepts built into the processes early on provided for change as knowledge over time was acquired and attracted the highest levels of expertise. A highly participatory process with a full range of expertise and interest all have contributed to its success. These check and balance processes have assured that it is not self serving, but has addressed the needs of society broadly in this area.

Research projects that envision potential release into the environment under controlled research conditions, or ultimately broad release, have built into them at an early stage extensive study and review of the molecular ecology involved. Furthermore, biological containment and gene performance in increasingly complex environments are tested under controlled conditions. Specific environments, genetic drift, and gene wearing in mixed systems are tested under controlled conditions. The multitude of naturally occurring genetic accidents and the resulting potential for interaction, as well as ecological gene training and attenuation are similarly tested.

Thus the resulting plant, animal, or microbial biota to be used in agriculture, wherein recombinant DNA technologies have been employed in their development, are not inherently different in nature than those we have used in the past. These resulting products should not be treated differently.

In summary, I have outlined the evaluation and oversight activities involving research and field experimentation with genetically engineered organism.

Mr. Chairman, this completes my prepared statement. I will be pleased to respond to any questions you may have.

STATEMENT OF

DR. ALEXANDER MacLACHLAN

DIRECTOR, CENTRAL RESEARCH & DEVELOPMENT DEPARTMENT

E. I. DU PONT DE NEMOURS AND COMPANY

BEFORE THE

TOXIC SUBSTANCES AND ENVIRONMENTAL

OVERSIGHT SUBCOMMITTEE

OF THE

COMMITTEE OF ENVIRONMENT AND PUBLIC WORKS

UNITED STATES SENATE

SEPTEMBER 25, 1984

Introduction

Good morning, I am Dr. Alexander MacLachlan, Director of the Central Research & Development Department of Du Pont. This Department has the responsibility for doing most of the Company's long-range basic research and for the introduction of new technologies to the Company. I have a Ph.D. in organic chemistry and have been with Du Pont for 27 years. As requested by the Chairman, my remarks are directed to a discussion of Du Pont's involvement in biotechnology and the Company's perspective as to how the government should go about regulating this science and its products.

Du Pont's Biotechnology Involvement

To put biotechnology into perspective, Du Pont, this year, will have sales in life sciences, including pharmaceuticals, radiopharmaceuticals, X-ray products, diagnostics and agrichemicals, at a level of about $2 billion. However, we have not, as yet, sold any genetically engineered products.

At the outset, let me define what I mean by "biotechnology". As I use this term this morning, "biotechnology" describes the directed molecular manipulation of genetic material, often referred to as genetic engineering. I wish to contrast this test tube splicing of DNA and its introduction into cells to make useful products with more traditional plant and animal breeding approaches. We see

biotechnology as helping us to produce new products that can compete with those made using traditional technologies.

The United States has taken the lead in the broad area of biotechnology at the present time. We believe that biotechnology's most immediate and dramatic impacts will be in human health care and in agriculture. In the area of human health care, the ultimate objective is a disease-free society. Biotechnology will help us to develop new diagnostic approaches as well as to produce new and more pure vaccines and hormone-derived drugs. In the area of agriculture, genetic manipulation and cell culture technology will lead to improved crop varieties that are resistant to diseases, pests and environmental stresses. Most important, plants that produce more food and even new crops will be developed through biotechnology.

Over the past five years, Du Pont has committed $150 million of capital investments in biotechnology research facilities. We made this decision for several reasons. First, we expected the new biotechnology to make a significant impact in our current and future life science based business--diagnostics, pharmaceuticals, agrichemicals, as well as in our commodity chemical businesses. Second, we recognized that the techniques of biotechnology were essential for research in any life science area and that the understanding from use of the

techniques indirectly would lead to major new products and processes. Third, we expected to engineer cells that would produce products and also, in the longer term, would themselves be products.

In short, Du Pont has a major stake in the life sciences research effort. We have invested substantial human and financial resources in this business sector.

Government Regulation of Biotechnology

With this background on Du Pont's efforts in the field of biotechnology, let me now turn to Du Pont's view of how the government should regulate this emerging business field. We believe that regulations governing the introduction of bioengineered organisms into the environment and the manufacture and distribution of products utilizing recombinant DNA technology are inevitable and will be implemented. It is necessary to distinguish, however, between the control of science and the regulation of industrial products and technology. Regulatory approaches should protect the public interest but should not place undue burden on this emerging industry. We do not believe that the external control of basic laboratory science in biotechnology is advisable or necessary beyond the precedent established by "RAC", the NIH Recombinant DNA Advisory Committee.

Insofar as I am aware, academic, government and industrial laboratories have operated, since 1976, under the safety and reporting aspects of the NIH RAC guidelines. The prevailing conviction of the scientific community, and the

view that Du Pont supports, is that the NIH guidelines, together with RAC's case-by-case review of laboratory experiments, are a thoroughly sound basis for ensuring public and environmental safety.

While the NIH guidelines are adequate for basic molecular biological research, they do not address adequately concerns about industrial activity in this field. Moreover, NIH currently does not have the resources to oversee the commercial development of biotechnology products. It is questionable whether taking on such a responsibility would be consistent with the Institutes' mission.

Consequently, products arising from recombinant DNA research, and the development of markets for these products, is proceeding without clear regulatory oversight. In Du Pont's view, such oversight should be the responsibility of a government agency or agencies with full regulatory powers. Leaving biotechnology in a regulatory limbo subject to the uncertainties inherent in lay review by our judicial system is unacceptable.

Clearly, there is an expectation that the U.S. will achieve commercial breakthroughs in biotechnology. It is our view that Congress has been supportive of biotechnology and, we understand has wanted existing agencies to oversee its development in a manner that will not stifle either scientific or industrial innovation, or compromise our current leadership position opposite the strong competition we can expect from other nations.

Several government agencies already have asserted jurisdiction over biotechnology in their areas of administration. The Food and Drug Administration has jurisdiction over drugs, devices and food additives. The fact that such are genetically engineered organisms or are produced by genetic engineering should not affect this jurisdiction. The EPA has jurisdiction over pesticides. Again, the method of action or manufacture of these materials should not alter the established authority. EPA also has responsibility for administering the Toxic Substances Control Act -- TSCA -- which gives it broad authority to regulate and monitor a wide range of industrial products and processes. Thus, EPA would also have jurisdiction over industrial application of biotechnology relating to the manufacture of a chemical substance. In addition, the Occupational Safety and Health Administration has jurisdiction to regulate the workplace and could fill any voids in the jurisdiction of other agencies.

Many of these agencies have already indicated that they believe existing laws provide them with the authority to regulate biotechnology and we do not challenge this. However, no agency other than NIH has yet established guidelines or protocols to deal with the special concerns that revolve around the intentional release of genetically engineered organisms into the environment. That is, no other agency has expressed its approach to open air field testing, development work or marketing of such products. And, under the present circumstances, even the well-intentioned

efforts of the different agencies involved could quickly become a collection of overlapping and redundant laws if we are not careful.

To avoid this, there should be systematic coordination of regulation among the existing agencies. In our view the principal activities should include the following:

- First, there should be clear expression of jurisdiction by the involved agencies, that is, it should be proscribed which biotechnological products or processes fall under each agency's unique jurisdiction. We understand the Cabinet Council is encouraging such activity and we support early action on this item.
- Second, the agencies should establish guidelines based on the latest scientific information that would form a consistent basis for administrative regulatory oversight.
- Third, the agencies must develop scientific competence in biotechnology. Until this competence is developed, the agencies should consult with RAC.

Developing an appropriate science base will be particularly important for EPA since it appears likely that the initial regulatory work will fall within the scope of that agency. Of immediate concern is the future of experiments that involve field testing of genetically engineered organisms since such experiments are integral to the development work of many academic and industrial laboratories in this country. It is crucial that no time be lost in

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providing the guidelines necessary for carrying them out to realize the benefits of such tests to our agricultural industry.

- Fourth, we recommend the establishment of an inter-agency committee for biotechnology regulation assessment. This committee would serve as a sounding board for those subject to regulation, as well as environmental and other citizen groups. It would hear complaints and suggestions and be in a position to correct redundancies and overlap among agencies. This committee should be established for a specific term, and only reappointed to another term if circumstances point to a continued need.

- Fifth, an eminent individual of impeccable scientific creditials and administrative experience should be appointed special counsel to the President on biotechnology. This would provide the government with an independent spokesperson who could make policy recommendations and comment on regulatory developments with the assurance that his or her comments would be heard at the highest levels of government. The biotechnology counselor would also be in a position to promote the expansion and funding of biotechnology research.

- Finally, we recommend that there should be a strong commitment to maintaining the NIH Recombinant DNA Advisory Committee to continue to oversee laboratory research. RAC's proceedings represent an important intellectual and scientific resource, and as new regulations are proposed it would be unwise to attempt serious departure from the committee's precedents.

In closing, we believe that a clear statement of federal agency position by each involved agency is essential at the earliest possible time. This is necessary to give direction to industry and to give assurance to state officials charged with environmental and public health responsibilities that public concerns are being addressed. In so doing, there will be no need for regulatory initiatives at the state level which, we believe, have a great potential for inconsistent and potentially overburdensome approaches, and will distract this emerging industry from its prime objectives. Therefore, although we do not see the need for federal legislation at this time, we do see a need for strong Congressional support for the existing agencies, NIH, FDA, USDA and EPA, to promptly establish oversight mechanisms to ensure that biotechnology product developments are undertaken in a responsible fashion.

ENVIRONMENTAL CONSEQUENCES OF GENETIC ENGINEERING

MARTIN ALEXANDER

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The introduction of a radically new technology usually will have a number of uncertainties associated with it. This is true of genetic engineering, and it probably has been true of every markedly new technology, whether it was the use of fire by primitive societies, the industrial revolution of the nineteenth century, or the application of nuclear energy to peaceful pursuits. The proponents of these technologies, probably in the past and certainly at present, argue for the enormous potential benefits and the absence of uncertainties. These proponents are undoubtedly among the best spokesmen for the benefits; it is their field, and they know it best.

However, it does not necessarily follow that those that know a technology can also assess its risk. Is the industrial manager really the appropriate individual to assess the impact of air pollutants emitted from his industry? Is the chemist the most knowledgeable individual to evaluate the possible human health problems arising from the widespread use of chemicals? And, are the laboratory geneticists the most knowledgeable evaluators of the environmental problems associated with the deliberate release of genetically engineered organisms? These individuals know their technology and have much to offer to society by exploiting it, but one should clearly distinguish their knowledge of how to make use of a particular technology and the information needed to assess the risks from what they plan to do. Genetic engineering is not at all unique in this regard.

For the ecologist and the environmental scientist attempting to predict the risk of introducing new organisms into our environment, there is a high degree of uncertainty in anticipating the consequences of genetic engineering. Such an uncertainty apparently does not characterize many laboratory-based geneticists and representatives of industry, who rarely have an adequate base of information in ecology or in other environmental sciences. This uncertainty, however, is found among many scientists whose daily concern is the behavior of organisms in natural environments, as well as in those man-controlled environments that we use for food and fiber production. The degree of uncertainty surely is not reduced by statements by specialists in other disciplines who maintain that, even in the absence of data or convincing theoretical arguments, no problems exist. Uncertainty is not equivalent to a belief that there is, or will very soon be, a problem, but it is associated with a feeling that we are progressing along a course of action that may lead to minor or major problems, in the near or in the long term.

As an applied environmental scientist and a microbial ecologist concerned with agriculture and chemical pollution, I am convinced that genetic engineering has much to offer to society. I believe that we shall soon witness the introduction into farming operations of microorganisms that will result in better control of insects and improved growth of the plants we grow for food and feed. New varieties of crop species will also be developed by genetic engineering, and these will result in greater yields and higher quality crops. Genetic engineering will also aid in our attempts to improve animal production and to reduce the severity and frequency of animal disease. In the area of chemical pollution, genetic

engineering probably will provide microorganisms that more rapidly or more completely destroy a variety of pollutants in surface and groundwaters and in industrial wastes. Thus, I believe that assessments of the possible environmental consequences of genetic engineering must be approached in the context of the many benefits to be derived from these research and industrial activities.

If genetic engineering is indeed the wonderful technology that many of us believe, it will be used in ever more numerous ways, and the various approaches currently being developed will be expanded to include a variety of organisms, uses and environments. It has been stated frequently that no problems have arisen with the few techniques and few organisms that have been engineered to date, but the ever expanding scope of genetics and the new areas for practical exploitation will take us far beyond the few techniques and the few organisms on which genetic engineers have focussed their attention. The technology is so powerful that an enormous amount of genetic information will potentially be transferable to a vast array of different organisms.

In this light, I, as an ecologist, am not too bothered by the lack of information on the possible environmental consequences of the still infant field of genetic engineering. However, I am enormously concerned by the lack of a meaningful base of information to predict what might occur as the science develops and industry becomes able to transfer an increasing amount of genetic information from one organism to another.

Indeed, a review of other technologies indicates that there was little or no hazard in their early stages. For example, during the initial development of the chemical industry or at the time when the use of pesticides was

just beginning, little or no hazard existed for society at large and no threat was posed to major natural ecosystems, but as those technologies became more widely used and moved in new directions, the environmental and health problems became quite apparent. Thus, it is the ever growing number of organisms and the diversity of techniques that will be used in genetic engineering that increase the concern about our uncertainties and our lack of information.

Natural environments have a variety of checks and balances that prevent the many species and populations in our surroundings from being overly abundant or doing major harm to other species. The various mechanisms that are responsible for the balance among species in natural environments hold in check the many pests and disease-bearing organisms that these environments contain. It is these very interactions that prevent most organisms from one habitat from becoming established in another. These same mechanisms probably will destroy most of the engineered organisms that are deliberately introduced, just as they have eliminated most organisms that are transported from one environment to another. Because of these natural checks and balances, ecological or environmental upsets associated with newly arrived or rare organisms are uncommon.

However, these ecological upsets do occur. They take place under two circumstances. First, when the natural system of checks and balances is upset, as commonly occurs when virgin land is cultivated, when the homeowner plants a lawn, when a farmer uses large amounts of a pesticide, or when a dam is built. Second, when species not previously present in an environment are introduced into that environment. The establishment of these so-called exotic species is known to have occurred for sparrows

and many other birds, the rat and mongoose among mammals, the gypsy moth and many other types of insects, a host of plant species that are commonly called weeds, and microorganisms that cause major diseases of agricultural crops, trees, animals and even of humans. The successful establishment and devastating effects of these dissimilar organisms is amply documented. Although one might question the applicability to genetic engineering of our knowledge of the harm done by exotic species introduced into environments where they were not previously present, that information is much more useful then untested and often unconvincing hypotheses about the lack of establishment or effect of an organism whose behavior in nature is totally unknown. Thus, although the history of ecological, agricultural and public health disasters has a questionable relevancy to a completely new technology, the reliance solely on ecological theory expostulated by nonecologists seems to be even more tenuous. Ecologists are embarrassed to admit that they cannot predict whether a currently existing species will or will not become established when introduced into a new environment. If ecologists cannot make accurate predictions for existing organisms in a problem area that is ecological, how can a nonecologist make a convincing statement about a newly modified organism, one for which there is no environmental experience?

What then are the areas of uncertainty? What should we know in order to reduce the level of uncertainty arising from the planned, deliberate release of engineered organisms? Five areas of ignorance stand out.

First, will the engineered organism survive? Obviously, if it does not survive, it will pose no environmental, agricultural or public health hazard, but likewise, a nonsurvivor would be of little practical interest

to industry because it would have little market value. On the other hand, some organisms may persist only long enough to give the beneficial effect for which the organism was originally engineered yet still sufficiently long to pose a hazard. Such poor survival of many organisms that do injury before they die is well known; for example, the bacterium that causes cholera usually stays alive in nature for short periods, but its persistence is sufficiently long to constitute a major threat to humans.

Second, will the organism multiply? For many species, the few individuals that endure do not constitute a problem in agriculture, ecology or public health, but should they multiply and reach large populations, major disturbances become evident. For example, the few seeds of a weed species that may be released or the few individual insects that may escape present no problem, but their multiplication could easily be the first phase in a major upset.

Third, is the potentially deleterious genetic information transferred from the deliberately released organism to other species? The microorganism or higher plant that is released for the purposes of increasing food production or promoting environmental quality may not endure, but those traits that serve as the bases for concern might be passed to another organism in the same environment. In this way, injury might arise not from the originally released organism but rather from another species that has acquired the genetic information. Such gene transfer does take place and serves, for example, as the basis for decline in effectiveness of certain antibiotics used in medicine.

Fourth, is the engineered organism transported or disseminated to new sites? Frequently, the area where an organism is first introduced is not the place where it can do some harm. The original site may not

be receptive to its growth, or plants and animals that it may injure may not be located in the vicinity. Many microorganisms and plants fail to be transported for any distance from the point of their original discharge, but other species are widely dispersed and soon appear at considerable distances from the point of their first introduction. For example, microorganisms in a short period of time may be transported for tens, hundreds or thousands of miles, and farmers noting the spread of weeds and allergic humans also can attest to the capacity of plant seeds and pollen to move for considerable distances.

Fifth, will the introduced organism have a deleterious effect? This, of course, is the critical question, but answers to that difficult question do not have to be sought unless the engineered organism survives for an adequate period of time, is able to multiply, and can move from the place of its introduction to the place where it may do harm. It is my belief that most genetically engineered organisms will not pose problems because most will not survive, most that survive will not multiply, gene transfer is reasonably infrequent, most that survive and multiply will not be transported to a distant place, or most transported organisms will not have the traits needed to cause injury. The fact that most engineered organisms will fail one of these tests does not mean that all will. Which organisms will fail one or more of these environmental tests cannot now be predicted.

Indeed, our knowledge is so limited that it is not even possible to state the characteristics that result in failure or success. Large uncertainties exist in anticipating the environmental consequenes of genetic engineering because of these major knowledge gaps. Consider the case of

survival. Some attention has been given to the issue of survival of introduced but not of engineered organisms, and it is known that many microorganisms that cause diseases of humans, animals and plants and many introduced plants and animals fail to survive when introduced into an environment where they do not presently exist. However, some of these introduced organisms do indeed endure. With the little attention given to determining the basis for successful or unsuccessful establishment, it is not possible to provide meaningful predictions of whether a new organism will or will not survive in nature.

Consider the issue of multiplication. Surprisingly little attention has been given to explaining why some species multiply in nature, whereas others do not. This is especially true of the types of microorganisms that are likely to be the subject of genetic engineering. Microorganisms as a class multiply in soils and waters, on plants, and within the bodies of animals, but we can rarely say whether a particular microorganism will multiply in nature. Such evaluations are simple to conduct, and the absence of information is simply a reflection of the lack of attention given to the problem, either by researchers or by regulatory agencies.

Attention has been given to the possibility of gene exchange in nature, however. Laboratory tests of microorganisms, for example, suggest that genetic information may be exchanged in soils or waters, but even this information is limited and usually comes from studies under highly artificial conditions and with traits that are not of environmental importance.

We also have considerable information on the dissemination of organisms from one site to another. This knowledge comes from monitoring the spread of human, animal and plant diseases and, to a lesser extent, from

basic studies in biology. The available information shows that certain microorganisms and plants are transported enormous distances, and the spread of disease, the dispersal of pollen and the transport of a variety of microorganisms is amply documented. Nevertheless, even with this ample data base, few of the attributes that make microorganisms more or less susceptible to dissemination are known, especially among the species of likely interest to genetic engineers. Hence, predictions of the dispersal of a new organism cannot be made with any degree of confidence.

Uncertainty thus exists on whether an introduced organism will survive, multiply, transmit its genetic information and be transported to a site to where it may have an effect. Can we predict its potential for doing harm? The information on ecological upsets and on diseases of plants, animals and humans is abundant. Enormous numbers of human deaths have resulted from the introduction of microorganisms into regions where the people were not previously exposed to the harmful agent, and the decimation of the population of Indians in North and South America and of the original inhabitats of the Pacific islands bears witness to the susceptibility of previously unexposed populations. The responsible microorganisms were not deliberately modified genetically, but simple genetic changes that have occurred and do still occur in nature have been the prelude to major human diseases, as with the virus causing influenza. These genetic changes may not be too different from those that are currently of interest in genetic engineering. Agricultural crops have also often been devastated following the introduction of a new disease agent, and many of these disease-producing microorganisms are genetically very similar to species that previously had little effect on the farmer's crop. Various mammals, harmful rodents, plants that we now term

noxious weeds and other species have successfully overcome the barriers to establishment that exist in nature, and they have had major impacts on their surroundings.

It is my belief that the probabilities of survival, multiplication, gene transfer, dispersal and detrimental effects are quite small, and therefore, the probability of the final event in the sequence is even smaller. Nevertheless, I do not know how small is a small probability. Moreover, as genetic engineering uses new techniques, is applied to more organisms and is more widely used, an event that may take place one time in a thousand will occur because the type of event has been repeated one thousand times. Let me stress what I believe is a crucial point: in the absence of a substantive body of scientific information to allow for reliable predictions, and in the absence of data from tests designed to provide information on individual genetically engineered organisms, it is utterly foolhardy to anticipate what may, or may not happen, in nature.

The uncertainties on the possible environmental consequences exist because of the paucity of information on the ecology of organisms related to those of current or likely future importance in genetic engineering. Scientists notwithstanding, uncertainties will remain even as we gain more information, but at least the degree of uncertainty and presumably the likelihood of a problem arising will be substantially reduced as the information is obtained. The degree of uncertainty can also be reduced by data from appropriate tests mandated by a regulatory agency. Even with a wealth of scientific data, testing is important because science provides generalizations, guidelines and approaches, but exceptions to the rule are not exceptional. Science can reduce but surely not eliminate

the uncertainty. Hence, it is essential that a regulatory agency require a meaningful but not onerous series of tests to evaluate potential hazards. These tests would allow that regulatory agency to go beyond the generalizations derived from scientific inquiry and should permit an evaluation of potential problems not revealed by our generalizations.

I am excited by the prospects and benefits of genetic engineering. I am also impressed by how little we know of the potential behavior of deliberately introduced organisms. I believe that the considerable uncertainties that remain among scientists trained to understand the behavior of organisms in nature can be reduced very markedly. This can be accomplished by research designed to predict the behavior of organisms introduced into environments in wnich they are not native and by regulations that require industry to provide information to allow for assessment of safety or hazard. In this way, I believe that we shall be able to gain the benefits of an extremely important new technology while minimizing the risk to humans, agriculture and our environment.

Title: Safety Concerns Regarding Genetically Engineered Plants and Microorganisms to Benefit Agriculture

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SUMMARY

Predictions regarding the safety of a recombinant plant or microorganism for agricultural use should be based on our vast experience with traditional practices such as plant breeding and use of microbial inoculants. An introduced plant, bacterium or fungus containing foreign genes should present no greater environmental damage than such organisms without recombinant genes. Problems caused by introduction of foreign organisms such as kudzu vine and gypsy moth should not bear on safety predictions of an organism, currently considered safe, that has several characterized recombinant genes added to its genome.

Federal agencies are considering types of regulation needed to protect the public from possible environmental and health problems that might arise from the release of genetically engineered organisms. Concern has been expressed because several agricultural practices, such as widespread use of DDT over past decades, have caused serious problems. Also, movement of weeds and insect pests into new environments have created problems that have become difficult to control. Examples include the kudzu vine, hydrilla, gypsy moth, and Japanese beetle. Because of these experiences, it is necessary to consider potential effects from the release of organisms containing genes from unrelated genera. This article will focus on the use of genetically engineered plants and microorganisms (bacteria and fungi) to benefit agriculture. Other applications, to which the same principles should hold with regard to safety issues, include the use of genetically engineered organisms for mining and detoxifying chemical wastes and spills.

Economic and environmental benefits expected from agricultural use of recombinant organisms are great but these should be considered in relation to potential risks. By splicing foreign genes into plant chromosomes, it may be possible to create plants resistant to a wide array of pests. The hope and expectation is that they will lead to decreased use of chemical fungicides and insecticides, many of which are toxic to man. Use of recombinant DNA techniques may permit development of plants that utilize fertilizers more efficiently, thereby minimizing fertilizer run off into streams and lakes. In many crop species, a relatively narrow base or germplasm is presently used to develop varieties. There is concern that this has created genetic vulnerability to disease in particular. Genetic engineering can be used to introduce new genes and thereby increase genetic variability for the future.

Genetically engineered bacteria and fungi also have potential value. For example, Rhizobium strains isolated from many locations around the world are being applied to soils in large numbers so that legumes (e.g. soybean, alfalfa, clover), produce high yields without needing expensive nitrogenous fertilizers. Several approaches are currently being used to increase legume yields with genetically engineered Rhizobium. Other microbes also are promising candidates for use in agriculture (e.g. mycorrhizae, Pseudomonas, and Frankia), and there is a good chance that the value of these organisms can be increased through recombinant DNA technology as well as through traditional mutation and recombination techniques. As in traditional agriculture, the value of the new plants and microbes can only be assessed after they have been tested under a variety of field conditions. This report will focus on ways to predict the safety/danger level of an organism that has received several foreign genes.

PLANTS

Plants have been crossed (traditional "genetic engineering") by man for centuries. New variants resulting from such breeding have generally not been a problem. Most of our high-yielding crops, productive forest trees, popular ornamentals and garden plants have been derived through breeding programs. Some crosses include those that would not occur without man's intervention. Crosses in the U.S. between high-yielding midwestern U.S. corn and its wild ancestor, teosinte are examples. Species that do not cross-pollinate have been crossed without recombinant DNA technology, by many scientists around the world. Oats is a good example. Cultivated oats have been crossed with a number of wild species to increase protein concentration of seeds and to introduce resistance to diseases. Protoplast fusion between cells of plants that normally are unable to cross have yielded new variants. Also, plants obtained by mutation have frequently been planted in experimental fields with the hope of detecting useful new phenotypes. These experiments produce novel plants and, with the exception of mutated plants, the progeny are the result of uncontrolled recombination of tens of thousands of genes. The exact properties of progeny from most of these crosses are impossible to predict. Breeders do not take special precautions in testing these plants in the field because they rely on vast

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experience that has not produced serious problems. Compare plants derived from breeding programs with those derived through genetic engineering. In the latter case, a few characterized genes are added to the plant resulting in plants with properties relatively easy to predict.

One ecological concern is the inadvertent release of a new weed plant that will be difficult to control. However, the long and diverse experience of breeders and plant geneticists indicates that genetic crosses among non-weedy plants will not result in a problem. As we understand more about the genetic and biochemical basis of competition by weeds, it is obvious that a large number of reactions/genes must interact appropriately for the plant to display the properties of a weed (e.g. efficient seed dispersal, long seed viability, rapid growth in an environment not normally favorable to other plants). It is possible that hundreds or thousands of interacting genes are necessary for a plant to be a problem weed. Thus, the chance that a cross between non-weeds will yield a problem weed is expected to be exceedingly small. Most commercial field tests with genetically engineered plants will involve cultivated crops that have been specifically bred for high yield under intensive agricultural practices. As the crops are bred for characteristics favorable to agriculture, the competitive properties are weakened. Such crops, if left unattended, are not capable of competing well with other plants. Addition of a few foreign genes to these crops should not produce an undesirable weed.

Obviously, if weedy species are to be purposely genetically engineered, both the weed and recombinant derivative need to be considered in light of potential environmental damage. Whatever level of caution is currently used by scientists, who purposely plant weeds, seems to be sufficient for weeds that have incorporated foreign genes. Genetic changes in weeds, through man's activity, have occurred prior to application of recombinant DNA technology. Over the last decades, the use of certain chemical herbicides have caused uncharacterized genetic changes by which weeds have become herbicide-resistant. Any problems have been overcome merely by using a herbicide to which the weed is not resistant, thus removing the environmental pressure for maintenance of the resistance genes.

There is a very small chance, through genetic engineering with uncharacterized genes, that the resulting plant may produce a toxic secondary metabolite or protein toxin. For this reason, animal feeding experiments might be desirable before an edible crop is introduced commercially. Even through traditional breeding, however, toxin production can be a concern, especially when exotic plants are used in the breeding program. A good example is the high solanine content of potato varieties that had to be removed from the market. Several plants currently marketed have toxins (e.g. rhubarb, cotton, castor) and therefore need to be carefully processed. Plant toxins, whether polypeptide or secondary products, should be rapidly degraded and not accumulate in the soil or water supply.

There have been problems caused through traditional breeding, and those types of problems are expected to occur from plants arising from genetic engineering. For instance, certain popular corn hybrids turned out to be especially susceptible to the fungus, Helminthosporium. This resulted in the corn blight which destroyed a large portion of the U.S. corn crop in the early 1970's. Breeders are trained to be alert for this type of situation however. They had lines ready to quickly replace the ones susceptible to corn blight. Field tests, therefore, are necessary to assess the threat of pathogens and to check for undesirable characteristics of new varieties, whether they are products of traditional breeding or of genetic engineering.

One of the reasons that critics urge caution with regard to environmental release is

experience with problem plant species such as kudzu vine. This plant has been extremely difficult to control after its introduction in the southern U.S. Deliberate release of plants produced by breeding or genetic engineering bears no relevance to problems caused by importing certain foreign organisms. Those problems were not caused by changes in the genetic make-up of the plant, but rather by its introduction into a new environment. The species evolved over eons to be competitive (that is why it exists naturally in at least one environment). In that natural environment, a variety of factors such as other plants, pests and weather kept the population in check. It is important to realize that it is only a rare introduced species that causes problems. The majority of U.S.-grown crops were initially introduced from other parts of the world. The U.S.D.A. maintains large collections of wild members of our cultivated species to improve our crops. These collections are not normally maintained under strict quarantine.

MICROORGANISMS

Even though fungi and bacteria are very different than plants, similar types of analogies regarding safety can be made. From the early years in this century, certain microbes were grown in large volumes and, in many cases, became the bases of new industries. Examples include antibiotic, solvent, vitamin and amino acid production. Scientists have not been concerned that escape of these organisms will create an environment or health problem that is difficult to control. This lack of concern is based on scientific experience and the common observations of microbial behavior in the environment. A culture of or billions of cells of an uncharacterized microbe is added to the environment every time uncharacterized "microbial cultures" (e.g. a rotting orange) are added to the environment. Microbiologists are not concerned that such uncharacterized organisms will cause a difficult-to-control problem. In the last few decades, many pure cultures of bacteria and fungi (inoculants) have been added to soils or plants in the environment with the hope of finding useful applications; for example, oil and chemical waste removal, wood and straw decomposition, plant pest protection or plant growth stimulation. Mutant strains of such organisms also have been added to the environment. Again, no substantiated damage of significance has been caused through these practices.

There is no reason to think that a bacterium or fungus that is not known to damage the environment will cause environmental problems after it has obtained several characterized foreign genes. That a dangerous organism in the soil (e.g., Clostridium tetani) will become more of a problem after acquiring these new genes, from the introduced organism, also is remote. Certainly, microorganisms intentionally and unintentionally added to the environment have naturally exchanged genes with other microorganisms. Such organisms have moved through wind and water, as well as through man's travel, to distant places. Microbes without man's intervention, are continually sharing and rearranging genes through transposons, viruses, plasmids, etc. Random microorganisms generally are unable to predominate in new habitats because preexisting organisms already have evolved to successfully compete for these niches. In most cases, a microbe in nature grows far more slowly than it does in laboratory cultures; thus the newly introduced organism will probably have a difficult time surviving and an even more difficult time significantiy increasing and maintaining its population, whether genetically engineered or not.

What is the chance that a harmless microorganism can become a pathogen after it has been genetically engineered to be agriculturally useful? Studies with pathogens have demonstrated that many genes with interacting activities (usually not all linked to each other) are required for a microbe to cause disease, persist outside of the host, and be transferred to subsequent hosts. Most of these studies involved animal pathogens, but it is becoming apparent that the same is true for plant pathogens. The chance that one

could accidentally convert a microbe that normally is non-pathogenic to become a problem pathogen through introduction of characterized foreign genes seems to be very unlikely. Appreciation of this should minimize concern over problems with natural dynamic microbial gene exchange among uncharacterized microbes in the field.

Examples are known from current practices in which acquisition of a single gene or a mutation in a microbe might cause ecological problems. Paradoxically, genetic engineering may be able to help in addressing those cases in which agricultural practices have had adverse environmental impact. Current applications of certain herbicides or pesticides to soils enrich the soil for microbes that degrade the chemical, resulting in the need to apply more of the chemical in subsequent years. Another example is aquisition of antibiotic-resistance genes that have caused major medical problems. These problems arose, not by man's ability to genetically manipulate organisms but, rather, by introducing chemicals to the environment. The problems can be reversed by eliminating application of such chemicals. In fact, some current genetic engineering experiments are focused on projects expected to decrease the use of many industrially produced chemicals.

NEED FOR FIELD TESTS

To allay concerns regarding the safety of a recombinant organism, it would be useful to follow testing protocols before the organism is released. However, the task of designing relevant tests for most situations seems to be enormous, if at all achievable. How would a greenhouse test show that a corn line resulting from a standard genetic cross will not become susceptible to a fungal disease or become a problem weed? If a bacterium increases corn yield in the greenhouse, how will we guarantee, without field testing, that it will not unexpectedly harm the following season's crop? Tests aimed towards predictions of microbe persistence level in a field could be very different and not relevant. Because different soils, soil treatments, and weather conditions can alter the growth rate and persistence of a microbe, greenhouse or growth chamber experiments probably have little relevance to field results. Experience with current field testing practices seems to be the best guide to predict safety.

Certain microorganisms and plants have been introduced in the environment without need for regulation. Such organisms containing recombinant DNA should not be of concern unless the introduced genes have obvious potential problems (e.g. botulinum toxin gene) which require special precautions. It is unlikely that such experiments would be proposed for field testing. Because of the complex interaction of genes required for an organism to cause disease or environmental disruption, it would be extremely difficult to purposely engineer an organism now considered to be safe to become an organism that would spread a significant problem. A program that aims to utilize, in agriculture, a plant, bacterium or fungus considered to be safe, but with several foreign genes, should have essentially no chance of accidentally producing an organism that would create an out-of-control problem. The chance and severity of a problem from genetic engineering should be compared to known problems from current genetic and chemical practices such as breeding and use of chemical pesticides. Regulation over release of genetically engineered organisms should be based on scientific experience and debate of the issues. This article, hopefully, will be used as a stimulus for debate.

THE POTENTIAL ENVIRONMENTAL CONSEQUENCES OF GENETIC ENGINEERING

THURSDAY, SEPTEMBER 27, 1984

U.S. SENATE,
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS,
SUBCOMMITTEE ON TOXIC SUBSTANCES
AND ENVIRONMENTAL OVERSIGHT,
Washington, DC.

The subcommittee met, at 10:10 a.m., in room SD–406, Dirksen Senate Office Building, Hon. Dave Durenberger (chairman of the subcommittee) presiding.

Present: Senator Durenberger.

OPENING STATEMENT OF HON. DAVE DURENBERGER, U.S. SENATOR FROM THE STATE OF MINNESOTA

Senator DURENBERGER. The hearing will come to order.

Good morning everyone. Today is the second day of hearings on the potential environmental consequences of genetic engineering.

We indicated on Tuesday the topic is a difficult one. The technology itself is new and little understood by the lay public. It does have a certain science fiction quality to it. The term itself, genetic engineering, sounds a little Orwellian.

But laying aside any vague and unfounded fears of modern science, I believe we are correct in approaching the new genetic engineering technologies with prudent caution. We learn from experience. We embraced without question the burgeoning chemical industry after World War II, and in retrospect we should have been more skeptical. We should not have been so dazzled by the promise of better living through chemistry that we failed to anticipate injection wells, waste dumps, and a lot of other topics that have occupied our time incessantly in the last several years.

I think there is an analogy with genetic engineering. We are in a period of dramatic innovation in techniques and products. Those persons most closely associated with this innovation assure us that enormous benefits will come from it. I do not dispute that. But we also must look ahead to the potential harm that might result and do whatever we must do to prevent that harm. It is a tricky question: how to get at the benefits of genetic engineering while avoiding the risks.

Witnesses we have heard so far have tended to agree that the risk of harm from releasing genetically engineered organisms is small, but that it does exist. I understand today we will hear about some of the possible secondary effects of these technologies as well.

The question is one of dealing with uncertainty. And here the opinions we have heard thus far diverge rather sharply. One line of reasoning is that genetic engineering is merely a more precise way of developing a hybrid corn or a shorthorn steer. Nothing to worry about.

The other line of argument is that we are beginning to tamper with the fundamental blueprint of life in ways that are qualitatively and quantitatively different from the practices of the past, and we had better proceed cautiously because we do not know enough about how ecosystems work to know the consequences of this kind of intervention.

I do not expect that today's witnesses will extricate us completely from that quandry. But I hope they can shed some additional light on the questions I put forward on Tuesday: First, does genetic engineering present the possibility of significant harm to the environment? And second, is the existing patchwork of statutes, regulations, and guidelines adequate to prevent any potential problems?

In conclusion, I need to note that one of our scheduled witnesses, Mr. Thomas McGarity, is unable to be with us today due to an illness in his family. However, we have received an excellent written statement from Mr. McGarity. It will be made a part of the record. (See p. 114.)

Let me then ask all four of our witnesses to come to the witness table: Dr. David Jackson, senior vice president and chief scientific officer, Genex Corp.; Dr. Daniel S. Simberloff, Department of Biological Science, Florida State University; Mr. Jack Doyle, director, agriculture resources project, Environmental Policy Institute; and Mr. Jeremy Rifkin, president, the Foundation on Economic Trends.

We welcome all four of our witnesses. Your written statements will be made part of the record of this hearing.

You may proceed. We will start with Mr. Jackson.

Our rules are stay as close as you can to a 10-minute summary of your statement. We will take the statements of all the witnesses before we proceed to the questions.

STATEMENT OF DAVID A. JACKSON, SENIOR VICE PRESIDENT AND CHIEF SCIENTIFIC OFFICER, GENEX CORP.

Dr. JACKSON. Thank you very much, Senator Durenberger.

I would like to make a series of points in my testimony this morning. Let me tell you in outline form what they are going to be.

The first is that I believe that regulatory action regarding the products of biotechnology, including genetic engineering, should be directed toward the properties of these products and not to the technology which is used to produce the products. I believe that the focus of the present debate on genetically engineered organisms, as opposed to organisms, however they have been produced and whatever their properties may be, is misleading and will be counterproductive in a regulatory context.

Second, and following directly from the first, I believe that maintenance of the focus on whether an organism has been produced by genetic engineering or not will lead to inconsistent and ultimately indefensible regulatory policies.

Third, I would like to argue that the existing regulatory agencies and the statutory authorities which underlie them are an appropriate base from which to regulate products made using biotechnology, including genetic engineering, and that no new agencies are needed. However, I do think the existing agencies need help.

The fourth point I want to make is that a ban on all controlled introductions of genetically engineered organisms into the environment would be counterproductive both scientifically and as public policy, assuming that it is in the interest of this country to commercialize biotechnology in a responsible way and to preserve our lead relative to other countries in this extremely important technology.

Fifth, I would like to suggest that we have a very relevant historical paradigm for the present debate over information of genetically engineered organisms into the environment. This paradigm is often referred to as the Asilomar process. It occurred in response to a similar controversy in the mid-1970's concerning potential biohazards of genetically engineered micro-organisms. I think that the Asilomar process has a lot to teach us, and I hope we can learn from that illuminating experience.

Let me now elaborate on these points.

The first point I made is that the focus on genetic engineering is something of a "red herring." Many people believe that an organism that has been modified by genetic engineering is somehow wholly different from normal organisms or from variants of normal organisms which are obtained by conventional genetic mutation and selection programs or by conventional breeding programs, techniques that have been used by man for the genetic manipulation of his environment for thousands of years. In contrast, I would assert that it is simply incorrect to conclude that genetically engineered organisms are somehow a fundamentally different class of organism. It is true that it is possible to construct organisms using genetic engineering techniques which are modified in ways that could occur at most very infrequently in nature. But it is also possible to use the same genetic engineering techniques simply as an alternative and much more efficient means of constructing genetically modified organisms which were previously constructed by conventional genetic means.

In this latter case, it is perfectly possible that two different organisms, one produced by genetic engineering methods, another produced by what we would call conventional genetic methods, could turn out to be literally identical. In such a case I think it would be very difficult to argue that one organism should be regulated differently from the other, simply because a particular set of techniques had been used to construct it.

So, I present this argument to focus attention on an extremely important point: A rational regulatory policy regarding release of organisms into the environment must focus on the properties of the organisms and the products they make, not on the processes by which the organisms were modified. After all, it is the characteristics of an organism, not the techniques by which those characteristics were modified, which will be responsible for any environmental impact the organism may have.

Let me turn now to the second point, which is related. It is that if we do continue to focus on whether or not an organism is genetically engineered rather than on what its properties are, then we will get ourselves into a difficult situation, certainly with respect to a consistent regulatory policy.

I think the current controversy regarding the field testing of the so-called ice-minus bacteria, which I am sure you have heard about at great length at these hearings, can be used to illustrate this point. As you know, ice-minus bacteria are variants of either of two species of micro-organisms, Pseudomonas syringae and Erwinia herbicola, which lack the ability of the parent microorganisms to promote the formation of ice crystals in supercooled water. The ice nucleation activity of the parent micro-organisms is responsible for a substantial amount of the frost damage done to crops by temperatures somewhat below the freezing point, generally between about 24 and 28 °F.

These ice-minus variants, which occur naturally or which can be produced by modifying the parent micro-organisms using either genetic engineering techniques or conventional mutagenic techniques, do not promote frost damage on plants they colonize. Also, of course, if these ice-minus variants are sprayed on the plants at appropriate times, they are able to reduce the population size of the ice-nucleating parent micro-organisms to the point that frost damage is substantially reduced.

I do not think there is very much dispute about any of what I have said so far. The information about ice nucleation properties of these micro-organisms and their genetic variants has been obtained from experiments using naturally occurring ice-minus variants in laboratories, greenhouses, and, I wish to emphasize, in field trials in the case of naturally occurring ice-minus variants. Experiments with genetically engineered ice-minus variants in laboratories and greenhouses have confirmed that these organisms behave in the same manner as the naturally occurring ice-minus variants under those conditions. But, as of course you know, field trials of the genetically engineered variants are much in dispute and are presently prohibited.

The ostensible reason for urging prohibition of field trials of the genetically engineered ice-minus variants is that their effects are unknown and might be damaging to the environment. I think one is forced to conclude, however, that the real reason prohibition has been sought in this case is that the organisms are genetically engineered. As mentioned above, field trials with naturally occurring ice-minus variants, which have similar, if not identical, physiological characteristics to the genetically engineered versions, have already been performed. So far as I am aware, there have been no claims of any harmful effects arising from these field trials. Moreover, there is no prohibition on repeating these trials with an organism which has been modified by conventional techniques rather than by genetic engineering.

I believe that situations as obviously inconsistent as this make for bad regulation. If ice-minus bacteria are harmful to the environment, they should not be placed in large quantities into the environment, irrespective of how they are prepared. Similarly, if they

are not harmful to the environment, the fact that they have been prepared using genetic engineering techniques is immaterial.

Finally, I think it is worth noting that other biological techniques for reducing the damage caused by Pseudomonas syringae-promoted ice nucleation have also been developed. One of these techniques involves spraying crops with suspensions of bacterial viruses which grow on these naturally occurring organisms. These naturally occurring viruses, in killing a whole population of bacteria, undoubtedly introduce an ecological perturbation, and probably a significantly larger one than the introduction of ice-minus bacteria which differ from normal micro-organisms by only one or a few genes.

I want to emphasize that I am not here taking a position as to the relative safety or efficacy of the various biological approaches to dealing with crop damage promoted by ice-nucleating bacteria. What I am saying is that safety and efficacy should be the basis for regulatory action, not the mechanisms by which the organisms have been modified, unless, of course, those mechanisms can be demonstrated to affect safety and efficacy.

Let me now turn to my third point. It is that I believe that the existing regulatory agencies are an adequate basis for a consistent, evenly applied policy of regulation for the products produced by biotechnology. Most of the products which will be produced by biotechnological processes will fall under the regulatory purview of one of three agencies: FDA, EPA, or USDA. These agencies have a long history of regulatory expertise and they have the statutory authority to be able to regulate products in these areas.

The FDA has developed considerable competence and sophistication in the subject of genetic engineering and products which result from utilization of that technology. The EPA is clearly aware of the fact that it needs to develop such competence and is moving in that direction. However, my judgment is that the EPA certainly needs additional help in the form of additional personnel who are expert in such fields as microbial ecology and molecular biology in order to gain the internal competence they will need to develop and implement a rational regulatory policy for the many new products made possible by biotechnology which will fall into the agency's regulatory domain.

I think there is also a question as to how best to use all of the resources of the Federal Government in the next several years while the regulatory agencies are developing their own internal expertise. Here I would suggest that a body already exists, the Recombinant DNA Advisory Committee [RAC], which could usefully make its expertise available to the various regulatory agencies. I cannot suggest how structurally within the Government one ought to make this competence available. However, I would suggest that functionally the situation that one would like to create is to utilize the competence of the RAC, which I think has real expertise in certain areas and lacks expertise in other areas dealing with the regulation of genetically engineered products and organisms, and supplement that competence of the RAC with people both from outside the Federal Government and from within the relevant regulatory agencies.

As I say, I cannot really make a recommendation as to how to achieve this goal in a structural sense within the Government, but functionally it seems to me that getting the RAC together with people from FDA, EPA, USDA, along with some people from outside the Government, particularly in the area of environmental science, could then produce a very important nucleus which could be used to help all of the agencies deal with the flood of decisions about biotechnology products which is bearing down on them.

Let me now turn to my final point, which is the historical paradigm from which I believe we have much to learn.

Back in the mid to late 1970's, there was considerable concern about the possibility that genetically engineered micro-organisms could infect people and animals and do so in a way that would be very difficult to control. A conference held at Asilolmar, CA, was convened to examine these questions. From the Asilomar Conference, helped subsequently very much by the leadership of Don Frederickson at the NIH, came a way of dealing with questions of unknown biological hazards that is something I think we ought to look at carefully.

Basically, I think what we learned from that experience is the following. The first lesson is that scientific input from many disciplines is extremely important in considering these questions. I am a molecular geneticist, but I would certainly not argue that molecular geneticists have all of the answers that are required to inform responsible regulatory policy in this area. I think we have to get people in who are expert in environmental sciences. We have to get people in with public health expertise. We need to be able to draw on the relevant expertise of soil scientists, water scientists, and atmospheric physics scientists. Indeed, I would argue that the Asilomar experience teaches us that it was not until the molecular geneticists and biochemists involved in the discussion specialists in infectious disease, epidemiology, and public health, that a lot of the noise that in resolving some of the most controversial questions hindered real progress got quieted down. It got quieted down because these people had the facts that were necessary to say what was real and what was not.

The second important point that we learned from the Asilomar experience is that it is relatively easy to set up scientific paradigms, experiments that can be used to test the underlying assumptions for some of the more horrible sorts of scenarios which were being put forth at that time. Those experiments were done under carefully controlled conditions in a period of about a year to a year and a half after the debate really heated up. What they showed was that indeed a lot of the assumptions that underlay the scenarios that predicted a great deal of harm were simply not valid and could be experimentally documented not to be valid.

Those results reassured many people, including a lot of people in the molecular biology community whose intuition had told them the potential problems were being greatly exaggerated but who really could not prove that their intuition was correct. The bottom line is that it is always useful to do the experiment and get some real data, instead of continuing to argue on the basis of different intuitions. Fortunately, it is often rather simple to identify and perform a few key experiments, the data from which can clarify

whole sets of major questions and which can thus provide the basis for intelligent future action.

Finally, I think what the Asilomar experience showed us is that we cannot insist on zero risk. We have to be willing to accept some risk. A scientist has to be able to get additional data which will provide the basis for greater certainty about risk and safety. The only way of getting such data is by performing experiments. By definition, one does not know how an experiment is going to come out ahead of time. So one has to be able to accept some small measure of risk in order to get the information that will make it possible to construct and implement a public policy that is rational and one which is based on intuitions and emotions. We should be getting on with the job of identifying and performing the key experiments relating to large-scale release of genetically modified organisms into the environment so that a regulatory policy having a sound factual base will be possible.

Thank you.

Senator DURENBERGER. Thank you very much, Dr. Jackson.

Dr. Simberloff?

STATEMENT OF DR. DANIEL S. SIMBERLOFF, DEPARTMENT OF BIOLOGICAL SCIENCE, FLORIDA STATE UNIVERSITY

Dr. SIMBERLOFF. I want to thank you for inviting me to testify at this subcommittee.

I am an ecologist. My expertise is in the organization of ecological communities—how animals, plants, fungi, microbes, et cetera, function together in nature.

There is a popular image of nature, called the balance of nature, that pictures communities as stable, saturated entities, with all ecological niches filled and no room for new organisms—either new genetic types of native species or new species from elsewhere.

In this view, natural communities are robustly organized, with each species held in check by its interactions with predators, parasites, disease and competitors. So in this view a new organism would be very unlikely to be able to insinuate itself into a community. There would be very few resources available for it. It would not be adapted to deal with the many enemies that it would encounter.

Unfortunately, ecologists have amassed lots of evidence that that is not really the way nature is organized and that if the right genetic type of a native species or the right introduced species happens to come along, it is able to fit into a community, even though it might be to the detriment of some original species.

I have heard the claims that introduction of a new species is not a good analogy for the release of genetically engineered organisms, on the grounds that genetically engineered organisms are native species, so they will be subject to all the controls from various interacting species and the environment that they have evolved with through the ages, and so they are much less likely to become problematic than are introduced species.

To me this seems to be a very false dichotomy. In either case, the community will have to deal with the new entity. It doesn't matter to the community exactly how that entity arose. There is not even

any valid evidence that introduced species are on average more harmful than new genetic strains of native ones. But just to be very conservative, I would like in a moment to give you some examples of native species that have undergone relatively minor genetic changes and have very rapidly become major pests.

But before I begin, I would like to point out that some of the genetic enqineering research that is currently underway is aimed at bringing about exactly the sort of change that in the past seems to have released native species from some sort of control and rendered them a real problem.

For example, there are now attempts to increase the resistance of plants to insects and disease. There are attempts to increase the geographic range or the virulence of diseases of insect pests, to extend the range of physical conditions and sometimes chemical conditions that will allow plants to grow, and attempts to broaden the range of substrates that will support the growth of micro-organisms.

Some examples of native species that have become pests because of minor genetic change come right to mind. One that is obviously topical is the bacterial canker that is now threatening the State of Florida's citrus industry with billion dollar losses. As far as we know, and the latest news is exactly one day old, this is not a bacterium introduced from another country. We know the bacterium was here. It is not even a strain introduced from another country. As far as we know, it is a mutation that occurred in the State of Florida. It could have happened anywhere, but it happened to have happened there.

There are other examples in the more classic literature. A good example is the apple maggot, which is a fly that until 1865 was only found on hawthorn. It was never found on apple. Then suddenly it was reported attacking apples in the Hudson River Valley, and then in a couple years New England, and by now, a century later, it has spread all over the Eastern and North Central United States.

It is a major economic pest. There is very good evidence that this host shift from hawthorn to apple was the result of a single mutation, allowing the larva, the maggots, to mature on apple, whereas before it required hawthorn.

The rice brown planthopper is another very well studied example. This is a bug that is a terrible pest of rice in Asia. Until recently it existed in Asia where it is native but was a very minor problem. Then in the early 1970's, there was suddenly a devastating outbreak of it in the Philippines. The bug itself began to cause more damage and to transmit harmful viruses. Over a few years it spread to Indonesia and then to India and now it covers much of Asia.

There has been extensive study of this insect, and there is excellent evidence that what happened was that a new gene arose, a mutation, that made the insect much more virulent.

The southern corn leaf blight is another example dear to the heart of many southerners. This is the fungus that devastated the corn crop in the South in the 1970's. After having been present and not having caused much problem, exactly why it became a pest in 1970, a major pest, we don't know, but we have very good support-

ing evidence that part of this was genetic change. It is known that at exactly the same time it became an economic crisis, there was a genetic change in the fungus that caused very different effects on the plant.

As a final example, from vertebrates, the collared turtle dove was restricted to the Balkans, a small part of the Balkans, until the 1920's. Suddenly it began to spread like wildfire throughout Europe and into Asia Minor. Now it covers all of Western Europe and much of Asia Minor. It has been a very serious pest.

The expansion occurred in spite of tremendous hunting pressures and other measures aimed at slowing it down. Exactly what happened we don't know. We don't have nearly as much evidence as we have in the case of the rice brown planthopper or the apple maggot. But Prof. Ernst Mayr of Harvard University, who studied this case, believes that a mutation changing behavior of the bird slightly is at the root of this.

I could give a number of other examples, but I think these should establish that a small genetic change in native species can lead to great ecological and economic problems.

One can also see how small genetic changes even in native species can be very damaging by looking at how pesticide resistance has arisen in hundreds of insect pests just over the past few decades.

Time and time again we have the situation where a chemical controls the population for a few years, then a resistant strain of the insect develops by a mutation, natural selection occurs, and control is lost. So we have to find a new chemical and then the process begins over again.

There are several insect species, including some mosquitoes, that are resistant now to every chemical we can throw at them. The development of resistance is a grave agricultural and public health problem. In some instances we are even worse off now than when we began using pesticides because the natural enemies of some of these pests have not been able to develop resistance and they have been locally eliminated.

The important thing to know about the development of resistance is that it usually rests on a very simple genetic change; in fact, often a single gene. This can come about in several ways. It can be as simple as a behavior change, causing the insect to sit on the bottom of the leaf instead of the top of the leaf so an aerial spray doesn't reach it, or it can be a mutation that detoxifies the pesticide so it is no longer a problem, or it can change an enzyme that had been damaged by the pesticide so that the enzyme itself is resistant. There are other ways in which resistance arises, but they are all very minor genetic changes, often involving single genes.

I do not mean to leave the impression that most genetic changes that happen in nature are bad problems. We have very good evidence that most mutations are never even propagated. They render the organism less fit and they disappear. I think this is probably what is going to happen to most genetically engineered organisms, in spite of the great ingenuity of the gene-splicers. But just as every so often a natural mutation causes the species to become a problem, it is quite possible, in fact, I think it is almost certain, that every once in a while a genetically engineered organism will

become at least somewhat of a pest, especially given the nature of the changes that are being envisioned.

I want to say a final word about introduced species. Most of them do not become pests. I have surveyed about a thousand of them that at least survived. Most of them don't even survive. We have no idea how many introduced species there have been. But of the thousand that survived, I found only about one-quarter that had some ecological significance. For many of those it wasn't much of an effect.

A few of them are well-known catastrophes: the Japanese beetle, the kudzu, the starling, et cetera. The only thing I want to add here is that some of these species and some other ones that are less obviously devastating, in addition to the obvious effects, like defoliating our ornamental plants or desecrating an orchard like a starling does, have very subtle ecological effects, like affecting production rates of trees or rates of nutrient cycling. These may be of very great economic importance, even if they are not obvious.

Now, what does all of this evidence suggest to me we should do about releasing genetically engineered organisms?

Since there are so many benefits that are promised by genetic engineering, in health and in agriculture, I think it would be foolish to try to stop it. In fact, I know it won't happen. There have been many introduced species that have been very beneficial. Many of our food plants are introduced species. So it would have been very unwise for us to try to stop introducing all exotic species.

However, the potential dangers from releasing genetically engineered organisms are probably about as great as those from natural genetic changes in native organisms or from standard conventional techniques of genetic engineering that plant and animal breeders have been using for a long time. I think they are probably as great as those from introduced species, on average. Since we can point to disasters in each of these areas, I think we really do have something to worry about.

However, I think that most of the disasters that arose from introduced species and probably also from naturally changed native species could have been avoided if there had been very careful study beforehand of the properties of the new genetic races or of the introduced species. I don't mean just running off a checklist of the properties of the proposed introduction that could be done by one technologist working for a week or even 6 months. I mean a full-fledged ecological study or study by a committee including ecologists and evolutionary biologists.

This would have to be done on a case-by-case basis, just as the FDA now assesses proposed new pharmaceuticals and the EPA mandates environmental impact statements. I think teams of specialists, including experts from the fields of ecology and evolutionary biology, could give very good advice and could minimize the risks of releasing genetically engineered organisms.

As in any risk-assessment procedure, it can never be foolproof and sooner or later an unforeseen consequence will occur. However, I think that this risk can be greatly brought down by having very rigorous testing procedures overseen by an appropriate panel.

I don't have expertise in organization of Government, so I don't really feel qualified to say whether this should be done in the con-

text of an existing agency or group of existinq agencies or whether something very different is needed. Of course, the FDA, EPA, the Department of Agriculture especially, and the NIH all already have expertise and responsibilities in rather similar situations. I am not yet confident that they would do this right. I am not saying they wouldn't, but I would like to see the proposed guidelines. I know that these are already being considered.

That is my final message. I think that lessons from the ecological literature suggest that there is definitely something to worry about here but that we should be able to minimize the major risk.

Senator DURENBERGER. Thank you very much, Dr. Simberloff.

Mr. Doyle?

STATEMENT OF JACK DOYLE, DIRECTOR, AGRICULTURAL RESOURCES PROJECT, ENVIRONMENTAL POLICY INSTITUTE

Mr. DOYLE. Thank you, Mr. Chairman.

I would like to thank the subcommittee for inviting us to testify. We appreciate the invitation. We commend the chairman and the members of this subcommittee for initiating these important hearings.

I must say that I didn't mean to intimidate the chairman or other members of the committee who may have seen my statement. Most of it is appendix. We hope that the full text will be entered into the record. I will proceed and try to excerpt from my prepared statement.

During the last 3 years at EPI I have been working on a book about some of the changes our society, our Nation's food and farm system, and our environment will likely experience with the application of biotechnology and genetic engineering to agricultural production. In the course of writing this book, which is scheduled for publication early next year, I have visited with numerous scientists and businessmen in the seed industry, at new biotechnology companies and established corporations. I have spoken or corresponded with hundreds of people in what might now be called the agricultural genetics business.

My discoveries so far leave the distinct impression that there is much promise with the use of new genetic technologies. However, there are also some clear reasons for concern and caution.

Advances and breakthroughs in the genetic sciences have occurred much faster than anyone anticipated, even as recently as 5 years ago. Huge sums of capital are being invested here and abroad, and a race has ensued among scientists, biotechnology companies, major corporations, and even national governments seeking technological supremacy in world markets.

Now in the United States, as genetically altered products draw nearer to commercialization, there is great pressure to secure swift Federal approval for these products. Yet, there has been little public debate on the potential environmental and social consequences of this new technology.

With the exception of the series of hearings held by the House Science and Technology Subcommittee on Investigations and Oversight, and its February 1984 report entitled "The Environmental Implications of Genetic Engineering," there has been very little ac-

tivity in Congress on this subject. Policymaking on the question of environmental release seems to be evolving more in the courts than it is in Congress.

While we may be in a period of deregulation and Government disengagement in some areas, it is our view that biotechnology and genetic engineering need to be regulated and monitored by the Federal Government.

There is every reason to be careful and cautious with the advance of this new technology and to question ironclad assurances that genetic engineering is so exact and precise that everything is under control and there is nothing to worry about. We have heard that once before.

As recently as 1970, plant scientists generally thought that the genetic traits that determine disease resistance and/or susceptibility in crops were contained in the nucleus of the cell. But after the southern corn leaf blight, which Dr. Simberloff referred to, wiped out 15 percent of the Nation's corn crop in 1970, scientists discovered otherwise. They discovered that cytoplasm, the liquid material contained in every cell, also had something to do with the genetics of disease reaction. They later learned that genetic information contained in the cell's mitochondria accounted for the corn's vulnerability. That was new information.

Today, as in 1970, we continue to learn new things about genes and how they act. Only in the early 1980's did we first hear the term "promiscuous DNA," meaning that DNA sequences could move about within the confines of the cell, in this case between chloroplasts and mitochondria.

Scientists studying this transfer activity at Duke University and the Carnegie Institution of Washington conclude that it is not a rare event, but a "general phenomenon." Before this discovery, scientists had assumed that intracellular organelles like chloroplasts and mitochondria were independent of each other. Now they know differently. But how the DNA gets from one organelle to another is still a mystery. So there is still an awful lot we don't know about the genetics inside of the cell.

Sometimes, however, it takes the scientific community a good while to accept such knowledge. In 1951, to the disbelief of her scientific peers, Nobel Prize winner Barbara McClintock first offered her discovery of "jumping genes." McClintock discovered that the genes on chromosomes, once believed to be stationary and therefore predictable in the genetic characteristics they controlled, could move or jump from one chromosome strand to another, thus affecting changes in the expression of certain traits. It took nearly 20 years for the scientific community to finally accept McClintock's discovery.

Today we are confronted with man-directed changes in this inside genetic world with new products being released themselves into the tremendous variability of the outside environment.

The available evidence here seems to indicate, as we have heard from Dr. Alexander and now Dr. Simberloff and others, that based on past introductions, most genetically altered organisms will not survive, but some will, and a few will create problems.

On the one hand, we have a science of ecology that is young, not yet predictive, in Dr. Alexander's words. On the other, we have a

bustling new industry ready with genetically altered microbes and other substances to be released into the environment.

In our opinion, it is not a question of whether Government should regulate, but how. To do otherwise would be to make the Federal Government an accomplice in an ecological crapshoot.

It is clear that a careful debate is necessary about how to regulate responsibly, one that covers all options and possibilities, and one that allays public fears and instills confidence that the new genetically created substances for agriculture, mining, enhanced oil recovery, industrial bioprocessing, and other uses will indeed be safe.

I might say that while fostering scientific and technological innovation are important, and important to our country and national leadership and international markets, so are public health and safety here at home and environmental protection, as well.

As the regulatory debate moves forward, there are some steps that can be taken, however. Federal research dollars allocated carefully to EPA, USDA, FDA, and the land grant universities can ensure that we have a predictive ecology in place before new genetically altered substances are released into the environment. In fact, Federal funds earmarked for biotechnological research might "build in" a predictive or consequences requirement as a part of all such grants, which would serve the purpose of inculcating such forethought into the process at the same time the research is being done.

But our concerns for environmental safety and ecological impacts go beyond establishing a sound predictive science base and a responsible regulatory framework. Our concerns also include the potential secondary impacts, the indirect environmental and agricultural consequences of biotechnology.

I would like to touch on a few of those, if I could.

At present, we are most concerned that some developments in biotechnology and genetic engineering might foster an increase in the use of pesticides in the environment and perhaps exacerbate in the long run some toxic substances problems, which I am sure this subcommittee is well acquainted with. Here, we are concerned about the genetic alteration of agricultural crops to make them resist herbicides.

Herbicides are chemicals designed to kill plants. However, few crops have the natural ability to tolerate the ill effects of herbicides. Some do, however. Wheat, for example, has an enzyme which naturally detoxifies the killing action produced by du Pont's new herbicide, Glean. Corn produces an enzyme which makes it resistant to the lethal effects of the herbicide atrazine. Yet, soybeans and alfalfa, two crops that might be used in rotation with corn, are not tolerant to atrazine. Similarly, sunflowers, sugarbeets, and lentils, crops that might rotate with wheat, are damaged by the herbicide, Glean. Moreover, these crops can be damaged by these herbicides even when the chemicals are carried over in the soil from previous applications.

But that is where biotechnology and genetic engineering enter the picture. Today scientists use tissue culture techniques in the lab to screen thousands of cells for potential herbicide-resistant survivors that may later be turned into new crop varieties.

For example, Monsanto's plant sciences research director, Robert J. Kaufman, testifying before a House subcommittee in June 1982, explained his company's work with alfalfa plants and the herbicide, Roundup:

> Alfalfa tissue was placed into culture first on solid media and later into liquid culture. In liquid culture, the cells were exposed to a lethal dose of the herbicide, Roundup, and the survivors were plated out for regeneration into whole plants. These new plants (or variants) were transplanted into the field and treated with Roundup the way a farmer would use the herbicide. Several variants were found to have field resistance to the herbicide.

Monsanto, of course, is not the only company now using biotechnology to help design crop varieties that will resist their own or other herbicides. In appendix A you will find a sampling of biotechnology companies and major corporations doing this kind of work, ranging from Du Pont to any biotechnology companies like Molecular Garrete.

One recent biotechnology companys' prospectus, for example, noted that some U.S. scientists working with tissue culture techniques have screened and selected out plant cells to regenerate plants with resistance to such herbicides as 2,4-D and paraquat. In a few cases, scientists have also cloned genes for herbicide resistance that might be moved into plants that don't have that resistance now. Such matching of herbicides with crop varieties genetically altered to withstand them will increase the use of those substances.

Not much is known about the long-term effect of herbicides in the environment. Although herbicides are generally not regarded to be as toxic as the chlorinated hydrocarbon insecticides used in the 1960's, they do have side effects. Not much is known about how herbicides completely break down, and according to some scientists, such information is only known for about four of the 150 herbicide compounds presently in use.

Herbicides such as atrazine have been found to cause chromosome breakage and other aberrations in plants. In fact, triazines, the chemical family to which atrazine belongs, generally are known to be mutagenic to some insects such as fruitflies. Moreover, recent revelations about one popular Monsanto herbicide, Lasso, which was recently found in Ohio drinking water, have raised questions about herbicide safety. Nevertheless, huge R&D investments continue to be made in herbicide chemistry, some of which is now buoyed by the prospect of genetic engineering.

Herbicide-resistant crops are one only area in a whole new world of agricultural chemistry that biotechnology may create. Research directors at many of today's leading chemical and pharmaceutical companies will tell you that they see a much more sophisticated era of agricultural chemistry ahead, one that includes plant growth regulators, encapsulated and synthetic seed, new kinds of microbial pesticides, viruses and genetically enhanced bacteria. Du Pont and Monsanto, for example, have both integrated growth regulator research with their plant genetics and plant biotechnology programs.

Some commercial scientists have told me that the reason they are pursuing herbicide resistance in crops is because it is easy, a single-gene change in some crops and one of the early gains of genetic technology. "You have to start with what is there to demon-

strate what can be done," one researcher told me. It is an understanding, he said, that will lead to other more sophisticated breakthroughs later.

Yet, herbicide-resistant crop varieties will be commercial products, and it is commercial products that this new industry wants most to show its stockholders, its underwriters, Wall Street and the media. While producing such products may be an innocent and necessary step along the path of genetic science, it will also be a highly capitalized step backed by a mass production system designed to recoup a return on investment.

Our concern here is with momentum, the commercial and scientific momentum that builds around any new and dynamic technology.

Senator DURENBERGER. Are you near the end, Mr. Doyle?

Mr. DOYLE. Yes.

Our concern is that a certain kind of product momentum will be set in motion in the earliest stages of this technology that may be difficult to turn around should something go wrong, difficult to reverse because of huge capital investments, scientific careers on the line, and accrued political support.

I would like to say a word about some of the impacts that this technology will have. Just to mention briefly, while I know it is off the subject a little bit, I think there will be some changes in the agricultural system that will result from the application of this technology. I would just like to raise a few of those examples here.

Just as we are now paying some attention to the potential ecological consequences of genetic engineering, we must also plan for social and economic changes that could come to agriculture and rural America with new technology.

For example, a genetically engineered bovine growth hormone enabling cows to produce 40 percent more milk on less feed could have dramatic impacts on the dairy industry. Some estimates have suggested that if widely used, bovine growth hormone would bring about a reduction of the Nation's dairy herd by one-third. That would mean a dramatic reduction in farmers and farm numbers. A similar development in the beef or pork industries would not only affect cattle ranchers and hog farmers directly but also feed grain producers nationwide. These changes, in turn, might lead to substantial changes in Federal farm policy.

To summarize, the Environmental Policy Institute finds that there are potential benefits and opportunities to come with biotechnology and genetic engineering in agriculture. There are constructive applications and inventions that can help to eliminate or reduce the use of chemicals in the environment, and these should be pursued sooner rather than later.

There should also be opportunities to diversify our agricultural production base through the use of new kinds of crops as well as ways to reduce the farmer's cost of production with disease-resistant crops and the development of hardier crops.

However, we also believe that there is need for great caution in the microbial realm, and that Federal regulation and funding for predictive ecology research are essential to ensure public confidence in this new industry.

Indirect and secondary impacts, such as those possibly resulting from herbicide-resistant crops, need to be considered, now, before capital investment makes their reconsideration later impossible. Perhaps EPA needs to play a more direct role in forcing the consideration of alternatives to products such as herbicide-resistant crops. By this I mean there is a need for some Federal role to look at alternatives in the biological area, for example. That might be one thing that Federal review agencies should consider in their evaluation of new agricultural biotechnology products.

Senator DURENBERGER. Are you at the conclusion? I have let you go 6, 7 minutes beyond the time.

Mr. DOYLE. I apologize. That is fine.

Senator DURENBERGER. Thank you.

STATEMENT OF JEREMY RIFKIN, PRESIDENT, THE FOUNDATION ON ECONOMIC TRENDS

Mr. RIFKIN. Good morning.

I would also like to thank the committee for inviting me to testify this morning.

Senator Durenberger, I would like to take a little bit of a different approach this morning because I think many of the issues that I would have raised have already been adequately raised by other witnesses. Since this is the first hearing of this type in the Senate dealing with genetic engineering and the environment, I would like to try and place it in a broader context, if I may, for a moment.

In 1973, that was the year of the energy crisis. Things have dramatically changed in terms of how the developed economies see long-range forecasting as a result of that banner year.

I would like to suggest that we are now seeing the first stages of a long-term transition over decades and perhaps several centuries out of the nonrenewable industrial type energy base into the renewable energy base, and biology is our chief focus for organizing our activity. This will become increasingly more relevant as the decades pass and biology will become increasingly more important.

The real question, I think, in front of this Congress, and it is also a question being debated by other nations right now, is how do we begin to approach the age of biology. How do we begin to restructure our relationships with nature. What is the economic implication of the approaches that we choose to use now. Those implications might not be well advanced until 50, or 75, or 100 years from now.

Now, I disagree with those people in the industry and the scientific community who say that genetic technology is simply an extension of the type of breeding or domesticating experience that we have availed ourselves of since late Neolithic man. In fact, it is quite different, qualitatively different. I venture to say the only parallel to the genetic technology that makes sense anthropologically is the harnessing of fire. For a long time human beings have been burning, forging the Earth's crust. We have successfully been turning it into all sorts of interesting things: steel, glass, cement, synthetics.

In the 1970's, the biologists came up with a new tool which is comparable in impact to fire technology, in my mind. The tool is

recombinant DNA. It allows you to take genetic materials from unrelated materials and recombine them, on a molecular level, that does not exist in nature. In a metaphorical sense, we can burn, sodder, forge, and heat, and cross all species boundaries and create new living products that never existed in the natural state.

Let me give you an example of what you can do in genetic technology that you can't do with normal breeding. Dr. Ralph Brinster at the University of Pennsylvania several years ago took a gene, a human growth hormone gene, and inserted it into mice embryo. The mice were born unlike any mice in history because they were expressing that human gene factor. Some grew twice as fast and twice as big. More interesting to me is the fact they passed the hereditary gene into their offspring so successive generations of mice have this human gene factor expressed in a very dramatic way.

There is no breeding measure in nature that we know of that can accomplish that fete. What I am saying is genetic technology allows us to eliminate species boundaries, species walls, the whole idea of the inviability, an arcane concept once we introduced recombinant DNA into our economic way of life. The sacred unit is no longer the species. It is the gene. In fact, it is no longer the gene. It is the information coded in the gene that can be synthesized by computer programming.

What are the implications to the environment for this kind of dramatic change in the way we relate to, organize and conceptualize nature?

First, we have to understand that biological products that are genetically engineered differ substantially from petrochemical products. A genetically engineered product is alive. We often forget that. Because it is alive, it is inherently more unpredictable and unstable in the way it might relate synergistically to its environment. They oftentimes will reproduce. They will migrate, grow. You cannot constrain them to a given geographical locale as you oftentimes can with a petrochemical product.

Third, a genetically modified product cannot be recalled back to the laboratory or be placed back into a drum or sealed up if it is on the microscopic level. Once it is introduced, that is it, and you have to live with the consequences.

Up to now, in the last year, we have been talking about a few experiments in the environment. But let's take it down the line 2, 3, 4, 5 years from now.

During the petrochemical age, we introduced thousands of petrochemical compounds into the environment each year. Most of them were benign. A small percentage of them were not. That small percentage has created a very difficult legacy for future generations to deal with. You eloquently addressed that, Senator Durenberger, in your opening remarks. It is very likely, in fact, I would say it is assured, that we will introduce thousands of genetically modified organisms into the environment each year, just as we did with petrochemicals. Probability suggests to me when you are introducing thousands of new genetically modified organisms into the environment, a small percentage of them are going to have possible problems associated with them. But unlike petrochemicals, the problems associated with living products could be irreversible, catastrophic and the legacy might not be one we can clean up.

Second, I think that we have to take a look at how genetically engineered products will impact other areas. Microbes have been a favorite topic over the last year, but let's take a look at plants.

What I am about to say is I am trying to make a broader point, that there is a myth to this revolution as we approach it in a animal husbandry and agriculture. The myth is if something is alive and reproducible, it is perpetually inexhaustible. We have had a long history with petrochemicals. They can be deleted and exhausted, we know. Unfortunately, most people believe living things are never run out because they reproduce. The central myth of this technological revolution in agriculture is you can get something for nothing.

Let me give you an example of why I believe living resources are as depletable and as exhaustible and as finite as fossil fuels. Let's take one example from genetic technology, photosynthesis. What if we could find a way to genetically engineer a plant so it would increase photosynthesis by 1 percent, so instead of 1 percent you get 2 percent. What would be wrong with that? That is the beginning of the food chain. It sounds terrific until you look at the consequence.

In order to absorb the increased ray of photosynthesis, we are going to have to apply more nutrients to the soil that would have to be used and absorbed in order to be able to compensate for the increased rate of energy flowing into that plant.

As you know, Senator, soil erosion and soil depletion is one of the major central problems facing our agricultural policy today. I am suggesting that if we radically increase the production, the yield of our agricultural products with genetic technology, we will run the risk of further depleting an already overtaxed soil base, leaving future generations with less ability to sustain agricultural crops than we have today.

Then, there is the crossing of species boundaries which no one seems to like to talk about. We are going to be seeing increasingly in animal husbandry, efforts to take genetic traits from one species and then interjecting them into the hereditary blueprints of unrelated species. There are potential long-term consequences, both environmental and philosophical, to this radical change in our animal husbandry policy.

First, on the environmental side. One could easily speculate that in introducing genetic traits from one species into the hereditary blueprint of another over decades and centuries that could do tremendous long-term harm to that species and perhaps not until it is too late and we see the damage done we might find the species itself could face extinction as a result of having foreign genetic material constantly forced into its hereditary blueprint.

Then, there is the philosophical question, which to my mind is an important one. Do species have any kind of right or inviability to their integrity of their gene pool? Are all animals here just as matter for manipulation? Obviously, we have to eat. I am not suggesting we reduce our diet to fruit and berries and nuts. But I am also suggesting the rest of the plant and animal kingdom has a certain inviability to their own genetic makeup. If we begin pall-mall introducing genetic traits into the hereditary makeup of species, for short-term economic and social purposes, we might in a sense

be undermining a very basic concept of our society, which is our long-treasured assumption there are certain sacred boundaries when it comes to plant, animal, and human life. I think that is something worth looking into in future hearings.

Then, there is to my mind the question of regulation. First of all, I think it is rather disingenuous to even talk about regulation at this point because we don't have a science developed to judge risk. Sometimes I feel I am an "Alice in Wonderland" on this issue of regulation. How can you judge risk in the various Government agencies when it has been acknowledged over the past few years we have never developed a predictive ecology methodology? We have no science and protocol to judge risk. In the area of petrochemicals, we have toxicology, and we can judge the risk of various products. When it comes to genetically modified products, there is no predictive ecology methodology.

The National Academy of Sciences 4 months ago was trying to gather some money to do a first study. I don't think we should go ahead and regulate until we can be convinced at least in some minimum way that there is a set of protocols, a scientific methodology, that would allow us to minimize risk.

I would suggest the best scientific talent in the country come together, not a token biologist or a token ecologist, but a cross section of opinions at the heart of the scientific community to see if they can't in fact come up with some kind of protocol for the development of this technology into the marketplace. If it turns out in the final analysis, by the way, we can't develop a science to judge risk and that it is too problematical, then I for one would say we should take the more prudent course of action and take the status quo against embarking on this radical change in the way we change nature.

Then there are international implications. To give you an example of how little thinking has been going on in some of these Government agencies, without naming names in particular, we have had several meetings on the international front now to discuss regulating this technology. In none of the meetings did they bring up the following problem. Countries like Germany, France, and The Netherlands are going to be introducing thousands of genetically modified organisms into their environment each year. Those organisms are not going to respect geopolitical boundaries like chemicals did. We have acid rain as a big problem now. Acid rain crosses boundaries.

What I am suggesting to you is genetically modified products, especially when you introduce thousands and thousands over years and decades, are going to cross all geopolitical boundaries. An organism you place in a southern France ecosystem that migrates to The Netherlands, it is fairly displaced. What corporation will be liable? What international body is going to deal with this?

It boggles my mind to try to imagine how we would determine liability for thousands of genetically modified products across all political boundaries in the coming decades. That has not even been addressed in the first international meeting we have taken part in.

Finally, I am very concerned about some statements in advance of this technology coming on line. I kind of feel like we are getting steamrolled into this biotechnical revolution with very little

thought. We have developed a shadow self. It is called the Japanese Nation. Whenever we have a problem here that we don't want to deal with, we say the Japanese are coming and, therefore, we better get moving. If it isn't the Japanese, it will probably be the Germans.

I am interested to note that Dr. James Weingarden at the National Institutes of Health made the following statement in Science magazine in August: "Biotechnology is coming to fruition. We can create a chilling effect and drive the industry abroad if we move toward too much regulation." I thought the Director of NIH's job was to look at research and the application of research, but I didn't believe his job had anything to do with commerce.

Secondly, Mr. Don O'Clay, who is Deputy Assistant Administrator at EPA, directing the agency's regulatory guidelines, said, "I am looking to regulate with a light hand." My God, they haven't even put out protocols yet. Here is an administrator of an agency announcing to the public in advance of protocols that "I plan on dealing with this with a light hand."

What I am suggesting is there is a feeling in this country now that chemicals are evil and bad, and living things are good. What I am saying is that genetically modified products are at least comparable to petrochemical products with the possible long-term impact they can have on the environment. To my mind, they are not only comparable, but they eclipse in a magnitude to any damage we have seen from the petrochemicals age.

We owe it to ourselves as a society, and we owe it to future generations to take a long, hard look at this radical departure and ask the question are we wise enough and smart enough to begin the process where we become the architects of life, the designers of a second genesis, the creators of our own living ecosystem? I for one have grave reservations about the whole thing.

Thank you.

Senator DURENBERGER. Thank you very much.

Gentlemen, Mr. Rifkin has just given us what I knew he would, a challenge. If I might start with you, Dr. Jackson, let me ask you to react to the comments that Mr. Rifkin has just made, I think particularly relative to the comparison with petrochemicals which he stretched out. I think he made several comparisons in that regard. Let me just ask you to react to his comments.

Dr. JACKSON. I must say I agree with some of Mr. Rifkin's premises. I certainly agree that the economic and technological impact of biotechnology is going to be at least on the order of magnitude of the impact of chemical technology, and not just petrochemicals, but chemicals in general.

Mr. Rifkin also said that when one introduces a large number of different genetically engineered organisms into the environment, the probability is that there will be potential problems with some of them. I have absolutely no argument with that statement. That statement is reasonable on its face. The real issues however, are what fraction of the organisms will present potential problems, how great are those problems, and how easy will it be to predict and either avoid or control them?

What I find disturbing about Mr. Rifkin's characterization of the technology as very hazardous is that by his own statement, there is

a vast majority of introductions of genetically engineered organisms which will not have potential problems associated with them. Since no one is doing these introductions just for the fun of it, one assumes this vast majority are going to have potential benefits associated with them. Are we to throw out a healthy, vigorously growing baby to get rid of a drop of bath water?

I think what we have to do is to be cautious in our introduction of these organisms into the environment. As several witnesses in these hearings have urged, we must support more research in ecology and environmental studies so we have a better knowledge base to predict when we are facing potential problems, and we have to proceed on that basis.

One of the points that I made is that the notion of a technology which poses zero risk to society is a will-o'-the-wisp. Pursuit of that will-o'-the-wisp is a prescription for paralysis. What we have to do is to seek for progress in ways such that we adequately protect ourselves while moving forward. I think we can do that in this area. I think we can and to a large extent have done that in the area of chemicals as well. We must not let the undoubted fact of some potential problems make us lose sight of the fact that there are also enormous potential benefits.

I have a little more problem reacting to Mr. Rifkin's comments about the problems of crossing genetic boundaries and integrity of gene pools and inviolability of species because I am not really sure exactly what he is suggesting.

If, for instance, he is suggesting, as he seemed to, that the introduction of genes on a consistent basis into a particular species of plant or animal was somehow going to unalterably modify that species in the environment and change it out of recognition, all I can say is that unless there is an extraordinarily strong natural selection in favor of the altered organism, what he seems to be suggesting simply won't happen naturally. It is impractical to go around and introduce the genes for some change into every corn plant or every field mouse in the world. That is so absurd I can't think that is what he is seriously suggesting.

I think it is also important in terms of Mr. Rifkin's references to the inviolability of gene pools and the sacred units of genetics to point out that one of the things that we now know is that the gene pool of organisms and species is not fixed but is in fact extremely plastic. We know this as a consequence of having done a great deal of basic research in molecular genetics over the course of the last 10 years. Genes and genomes which vary are found both in higher organisms, such as animals and plants, and also in lower organisms, such as bacteria and fungi.

Mr. Rifkin cited Dr. Barbara McClintock's work with corn, which was in fact one of the first instances where the plasticity of an organism's genes was demonstrated. We now know that such changes in genes and their organization in chromosomes is in fact a normal part of the developmental process of many organisms. In man, major and substantive genetic reorganizations do occur in some of the most important cellular systems in the body. For instance, in the immune system in man, such reorganizations occur as a normal part of development.

So to suggest that there is somehow an invariant gene pool which is engraved on a molecular scale on marble tablets and which is the unchanging genetic definition of corn or mice is simply not in accord with the facts as they have been established over the course of the last decade.

I would like to make one other comment at this point, and that actually refers to something that Mr. Doyle said. He said that people have given ironclad assurances that genetic engineering is so exact and precise that everything is under control and that we are able to predict all its consequences. I would like to make it clear that I do not share this view as stated and that I believe that, if such statements have been made, they are inappropriate. I think that no scientist should be giving those kinds of ironclad assurances that genetic engineering or any biological technique is such that we understand all the secondary and tertiary consequences of changes in organisms, particularly when we are talking about something as complex as interactions with the environment.

Now, with respect, I have not heard very many people stating what Mr. Doyle said they were. Rather, I think the argument has been that in a few specific cases we know enough about these secondary and tertiary consequences to permit careful experimentation regarding the ecological consequences of introduction of some organisms.

At this juncture, I want to reemphasize something I said in my testimony. If we don't do those kinds of experiments, if we don't try to get more facts, we will maintain ourselves in the state of ignorance we are today, which we all agree is not acceptable.

Senator DURENBERGER. Dr. Simberloff?

Dr. SIMBERLOFF. First, just as a fast response to Dr. Jackson. If you would like to see a claim of exactly the sort that Dr. Doyle said is afoot in the community, you might look at the letter by Bernard Davis, who is an endowed professor of bacteriology at Harvard Medical School in Genetic Engineering News in July and August, and also in Discover magazine, saying exactly that there is virtually no problem whatsoever.

In response to Mr. Rifkin, first of all, I am not a theologian or moralist so the questions about our rights of transgression of species gene pools I really can't address. But I think that on practical grounds Mr. Rifkin is correct, that it is not really fair to say that the sorts of engineering that are being done now and that are envisioned are really just part of the continuum of the sorts of things that plant breeders have done for hundreds of years. The aspect of transplanting genes, moving genes from one species to another, really is very different.

We have been able to hybridize species by conventional means, but they are almost always within the same genus. We could never envision moving a gene from a human to a mouse, which we have already done.

It is also true that occasionally hybrids of even closely related species in nature turn out to be real pests. A very good example is the radish of commerce, which is Raphanus sativus. That is associated with a wild native species, and the hybrid of this is now a pest in many parts of the United States. There are other examples of this sort I could give.

I think it might be very reasonable to expect that moving genetic material between more disparate, more evolutionarily disparate species could lead to very great problems.

A second aspect of the difference in the methods that are now in use is one that I do not really have expertise in. But I should mention that the specific way in which genes often are transplanted is by using plasmids, which are elements that as McClintock and others have shown move on their own, in addition to our moving them or putting them in a position in which they can be moved. So that it seems to me quite likely that once the genes are in place as planned, there may be a higher mutation or movement rate. This is something we haven't even thought about.

A final point is that the same technology that allows us to consider some of these remarkable experiments could probably also be put in the service of making them safer. As one example, microbes. We could put in leashes, genetic leashes, and we could dictate that in addition to whatever genes we want for other reasons, we would demand susceptibility to a particular chemical or to a particular virus, so that if something did get out of hand we could call it back because the strain we released was susceptible.

As Dr. Doyle said in a different context, we could, so to speak, ecologically disarm a new plant strain by insisting that it also be susceptible to an herbicide that we could later use in spite of our best field tests if something untoward happened. So I believe there is also reason for optimism.

However, all of these things will cost money. I don't think that the industry will be interested in doing them unless it really is forced to do them.

I have to respond to the contention of both Dr. Doyle and Mr. Rifkin that ecology is young and not predictive. Ecology is a young science. The first American textbook of ecology was only in the year 1900. So it is certainly younger than organic chemistry or physics.

But there have been very dramatic advances made, especially in the last 30 years. There is a large corpus of knowledge that we can draw on. I do not believe it is fair to say that it is not predictive. It is true we cannot in this instance provide you with a checklist so that we can say OK, the following five criteria have been satisfied, this introduced organism will not cause a problem. However, one has to remember that ecologists are normally dealing with budgets of a few tens of thousands of dollars and people call us up and say hey, what is going to happen if I release this fly, for example. I get phone calls of this sort.

Now, if I had sufficient resources even to fund one or two Ph.D. dissertations, for 2 or 3 years, to deal with exactcly that topic, I believe that 95 to 99 percent of the time I could provide a valid answer. I could be predictive. It would take a very close ecological study of the biology of the organism and it would cost perhaps several tens or maybe hundreds of thousands of dollars if we were dealing with a very large problem. The FDA, I believe, requires tests costing a few million dollars for a new pharmaceutical.

I believe that ecology generally has been hamstrung by the demand for quick answers to problems that are much more compli-

cated than the problems that physiologists routinely face. I think that given the appropriate resources, we could be predictive.

However, I must also concede that, as for any science, no matter how mature, like physics, risk assessment will never produce absolute certainty. There will always be some possibilities of a mistake. The best we could ever hope to do in any circumstance is to minimize that possibility. I think that with the right commitment, ecology could lower that probability to an acceptable level.

Senator DURENBERGER. I think the latter is an interesting point that I hadn't thought about in the 20 years or so that I have been associated with environmental sciences or ecology. I would suspect that the pressure on the science in the recent 20 or 30 years has been so great in a political sense that without totally adequate financial and maybe, in some cases, professional resources, the answer usually errs on the side of finding a problem because that satisfies the political pressures rather than on saying with a little more study we might come out with a different answer.

Mr. Doyle, do you have a collection of responses there?

Mr. DOYLE. Yes, thank you.

I would first like to correct the record. Dr. Simberloff's generous elevation of me to a doctor is appreciated, but it is not true, in fact.

But I would say, as to my reference of ecology as a young science, I meant to emphasize that the science of ecology is going to have to be rewritten anew because of the genetic element now; that the science of ecology is relatively young compared to some other sciences, but now it is changing very dramatically because of the genetic component. Certainly microbial ecology. I think in those areas there is some concern for learning new things in terms of the genetic variable.

After hearing Dr. Simberloff's remarks, I think that I should have said that the ecology is economically deprived rather than a young science.

With regard to Jeremy's remarks, I think something he touched on is very important. When he talked about photosynthesis and looking at the kinds of system requirements and how very small changes in a process or a cycle such as photosynthesis has to be looked at in detail, and all of the various impacts associated with increasing it or making a very small change in a process like photosynthesis.

I think similarly, we have to take very great care when we look at what is happening in the nitrogen cycle, or the carbon cycle for example. We have to have that kind of perspective as we approach the environment with new genetic ingredients that come in at one point or another.

One thing I did not get a chance to touch on in my statement, but I think it relates very strongly to the ability to regulate, and the kinds of checks and balances we have in science for evaluative purposes, I think today we are finding that there is a great scramble for talent in a few key areas, molecular biology particularly. We are finding that land grant universities throughout the country are being besieged by offers. Talented people are leaving the universities for jobs in industry. Let me mention one example that I think will illustrate how this affects agriculture.

A few weeks ago, I was visiting over the phone with a person in the seed industry from Oklahoma. Oklahoma is a State that has maybe 12 or 15 seed companies, none of which have their own plant breeding programs. They all rely on Oklahoma State University for their breeding lines. Wheat, for example, is a very important crop in Oklahoma.

This person from one of the seed companies in Oklahoma said that recently that Rohn & Haas, a Philadelphia pharmaceutical company that is very much engaged in developing a chemical hybridization technique for wheat, came to Oklahoma State University, hired away their top wheat breeder, and that has had an impact on the seed companies, and will eventually have an impact on the wheat lines coming out of Oklahoma State University.

Now that is just one example, but it is happening all over the country, and not only in the plant breeding sphere, but in other areas as well.

We have been a country, I believe, that has had in its land grant system—and private universities as well—a capacity of our scientists to play an important role in evaluating new kinds of products. I think the ability to do that kind of evaluation is being dramatically altered by this new industry, coupled with reductions in Federal funding to some of those areas of research. So I think that this is a very important area for concern, and one I would hope this committee would look into in the future.

Senator DURENBERGER. A couple of you have referred to, and I think some of this came out on Tuesday, the pressure of innovation and getting to the marketplace and so forth.

I understand that OTA, in a study they recently completed, suggested the importance of our being out in front in this area.

I wonder if, as briefly as possible, either each of you or whoever feels qualified to respond, and I probably should have asked this question of Tuesday's panel also, could respond to what are the economic pressures out there that make this new genetic engineering industry such a great thing to invest in?

I listened to the agricultural discussion and I saw the representative from USDA do the predictable thing—give us an illustration of productivity. Well, that is their business, productivity, however you might define it. They do a lousy job of assessing the cost of productivity, at least as I have noticed it in the last few years here, in terms of pesticides and soil erosion and a whole lot of other things. But getting more seed and more kernels to the cob and more plants per acre and so forth is what the U.S. Department of Agriculture is all about. I can't understand why the economic pressures are to increase productivity in agriculture.

From these hearings, because I haven't asked the questions, I don't have a very well-defined sense of where the economic potential is for all of this product that we are talking about.

We will start with Jeremy.

Mr. RIFKIN. If E.F. Hutton is to be listened to on this score, several years ago I believe it was Nelson Schneider, but I might be wrong, who said the biotechnical revolution will impact over 70 percent of the gross national product by early in the 21st century. We are talking here about a technology that can cruise the entire economic span, not just animal husbandry or pharmaceuticals but

packing materials, building materials. There is literally nothing that would be outside of the purview of using genetic technology. The pressures are enormous, even though the contradictions are apparent. I think you alluded to some of them.

For example, we pay farmers now not to produce. Now that genetic technology specialists are going to develop even faster more productive yields, we will pay farmers even more not to produce.

The same is true in animal husbandry where in so much of the field there is overproduction right now. Without going into the other fields, I would like to touch on one aspect of this that has not gotten any attention. I think it is safe to conjecture that the new form of international imperialism in the 21st century will not be oil, it will be germ plasm.

Right now multinational corporations are prospecting the far ends of the Earth to find wild strains and to try and locate control and manage germ plasm of the planet. This is going to be the gold, the oil of the 21st century.

I think the Third World nations as well as developed nations are going to be in a mad struggle, a very, very desperate struggle on the question of who should control genetic strains, et cetera. I think this is something I would like to see some hearings on sometime in the future because this will affect our national security interests, it will affect foreign policy relations, and it will affect our military objectives.

Senator DURENBERGER. Dr. Jackson?

Dr JACKSON. Since I was a member of the OTA panel that put that report together, let me try to respond to the comments about it.

I think the basic reasons for the economic pressures—I think perhaps incentives might be a better word—to invest in biotechnology is that it really does have extraordinarily broad potential applicability. Let me just give you what I think is an historical parallel.

Back a little over a 100 years ago a group of German scientists working in German universities laid the basis in the science of chemistry for synthetic organic chemistry. In doing so, they really transformed the science of chemistry from a descriptive science, which simply analyzed the world and described what it was made of in chemical terms, to one in which the technology was now present to allow one to change that world, to synthesize new compounds.

Out of that dawn of the synthetic age of organic chemistry came a German chemical industry which dominated the world for the next 50 years and which would probably have continued to do so if it had not been for the intervention of the First and Second World Wars.

There has been a lot of hyperbole about the prospects of biotechnology and genetic engineering, which is only part of biotechnology. But I really do believe that we are at an equivalent point with respect to biology. We are at the dawn of the syntehtic age in biology. That is what the techniques of recombinant DNA methodology and all the things that come along after it have really made possible. We are at a very rudimentary stage at this point, but the prospects for the future in economic terms are very much the same, in

terms of transformation of a whole field, as they were 120 years ago for the German chemists.

Now, what kinds of generic things can this technology do? Well, I would argue that you can think of it really quite simply. The technology will in many different fields, ranging from agriculture to pharmaceuticals to chemicals to energy, offer both product improvements and process improvements. Examples of product improvements might be some of the things that are coming on the market right now in the pharmaceutical industry, where by using genetic engineering techniques we can isolate and produce substances that you just could not get any other way. They are just too scarce in their natural state.

So there will be all sorts of novel products that come out of this technology, simply because these techniques enable us to access the entire gene pool of the biosphere. It is important to understand that the techniques of genetic engineering are very general techniques. DNA is the basic hereditary substance in every living organism. If you can get the DNA, these techniques are such that they treat DNA as a chemical, so you can isolate genes for any protein in nature from any organism in nature. So you will have access to a much broader range of potential gene products: enzymes, proteins, hormones, and so on.

But the other kinds of generic improvements offered by biotechnology are in some respects perhaps even more important. These are process improvements. They are things that affect the productivity of industries. That I think is an equally important economic incentive as to why it is people are so interested in biotechnology.

The kinds of things I am talking about here I think will show up first in the specialty chemical and food processing industries. An example would be the use of products and processes developed through biotechnology to increase the yield of a given product from a certain amount of feedstock. There is a clear economic advantage to the company that can do that. Another example would be is something which will enable the rate at which you can transform a given feedstock into a given product to be increased. That class of generic improvement has beneficial economic consequences for the capital investment in equipment required to produce a given amount of product, and hence a direct impact on productivity. Other techniques will enable one to use different and cheaper feedstocks to transform into a broad range of products. That too has obvious beneficial economic consequences.

To summarize: Biotechnology offers product improvements and process improvements which focus toward increased productivity. It is these broadly applicable, generic improvements that are the economic incentives in a very broad range of industries, and this is why so much money has been invested in this technology.

Senator DURENBERGER. I have to ask a series of other questions before we finish here.

First, Dr. Simberloff. In the Tuesday hearing one of the witnesses said that genetically engineered organisms will not be a problem because any added genes will be well characterized and we will know what specific traits, such as disease resistance, are being built into the receiving organism. I think Dr. Jackson made a similar point when he pointed out these organisms are likely to be

highly specialized and, therefore, even less likely to survive and multiply outside the specific environment.

I would like your reaction to those comments. Are these organisms less likely to present problems than the organisms in the examples that you gave us in your testimony?

Dr. SIMBERLOFF. I suppose a guess would be on average, yes, but maybe not as much as one would hope. It is true that the genes will be characterized. That will be an enormous advantage. However, I could point out that even in pesticide resistance, for example, many of the genes that have made the insects resistant have now been characterized and located. The insects are still a problem because they are resistant to the pesticide. I could give similar examples of weeds.

I think that on average the danger will be less. However, since many of the contemplated changes involve releasing an organism from some sort of previous control, the immediate consequence might not seem to be of economic or ecological, major ecological significance, but there may well be concatenated effects and subtle effects that only a very thorough ecological study could have predicted. There are many examples of this sort of thing in the literature.

So, I can't be cheered greatly by the fact we will understand the genetics of the situation better than we have for introduced organisms.

Senator DURENBERGER. Let me ask each of you if you are willing to address the subject, and do this probably in writing, to elaborate on the hearing record, for additional research to develop some kind of a predictive ecology. This subcommittee does have jurisdiction over EPA's research and development authorization. We have looked in this context into what everybody else is doing in the research area. If you could help us with your recommendations about what particular kinds of research needs to be done, what is already being done, and where it might best be stimulated, that would be an important part of our record, to the degree you are willing to do that.

My next question is of Dr. Jackson and Dr. Simberloff. On Tuesday Dr. MacLachlan of Du Pont called for regulatory review of intentional release experiments. Dr. Alexander of Cornell said some testing could be required in order to determine ability to survive and multiply. However, Dr. Alexander cautioned that predictive ecological testing is not at all exact.

I wonder if each of you would comment on the state of the art of this kind of testing and the wisdom of requiring testing. Is there any way to predict what will happen to an organism in the environment without actually releasing it to see what happens?

Dr. SIMBERLOFF. I believe that field, as opposed to laboratory testing for macroorganisms, plants and animals, would in many cases allow us to be very predictive. Now, because we are talking about a controlled field situation, in other words half an acre or an acre, rather than a laboratory, and we have to have stringent controls, this sort of work is not cheap. However, there is lots of precedent for field experimentation in ecology. Much of it is very ingenuous. There are already some protocols—for example, caging of plants—that have been very well established.

As I said earlier, given the appropriate commitment of resources, I believe that an acceptable level of prediction could be achieved and that this would probably be the approach that would usually be used, field experimentation.

Senator DURENBERGER. Dr. Jackson?

Dr. JACKSON. Since I am not an ecologist, but rather am a molecular geneticist, I have to defer to my ecologically trained colleagues. What Dr. Simberloff says seems to make a great deal of sense to me.

I, again just want to make the fundamental point that until one does field testing, and I think this is what Dr. Simberloff has said in other words, until one does field testing, one is really not going to have a good model system to be able to get the predictive capability you would like to have.

Dr. SIMBERLOFF. However, by field test I mean a controlled field test, before release. It is possible to control many organisms in very large field settings. It takes ingenuity and economic support. But this sort of thing has been done and could be done much more.

Dr. JACKSON. Yes, I certainly agree it should be a controlled field test.

Senator DURENBERGER. Dr. Jackson, you make the point it is the genetic makeup of the organism that matters, not the way in which the organism was developed. If we do decide that some form of regulatory review is needed, and we do not predicate the review on genetic engineering per se, how do you suggest we identify the few organisms that might require controls from the vast number of organisms that are developed each year? What is your handle, if you will, on this problem?

Dr. JACKSON. I think that is a very good question, and to answer it I want to take issue with some things that have been said before this morning.

I think it is essential to understand that genetic engineering is part of a continuum. That is not to say that there is not a previously inaccessible extreme end to the continuum which is different from what has been possible before. That is certainly true. And we have heard some examples of that this morning.

But it really is part of a continuum of ways of accomplishing changes in the genetic structure of organisms that ranges all the way from simply going out in the environment and looking for naturally occurring mutations and selecting those, all the way up through conventional breeding programs to the induced mutagenesis and selection programs which have been so effective in the pharmaceutical industry, and then finally to genetic engineering.

If you accept the assertion that it is a continuum, then I think a reasonable way to focus one's risk evaluation efforts is to ask where on the continuum is a particular organism or product that one is concerned with? Is it something like a bacterium which produces an enzyme that is already a product of commerce at a higher yield, and it does so because it is a genetically engineered organism and it is now more efficient at producing that particular enzyme, or is it a mouse that has human DNA in it and has some very unusual physiological properties that have not been seen before?

It seems to me that your first focus on your evaluation is to ask is this something that looks like something we know about, that we

have seen before? If it is, then there are probably in fact evaluative protocols that are already available that one can bring to bear on it.

I think one can in general—not always, but in general—feel relatively confident that you have the basic understanding that is required to evaluate such products or organisms.

If, on the other hand, the product or the organism is way out at the end of this continuum, it is something we haven't seen before, then it is in those circumstances that I believe a much more cautious approach is called for. In these cases, one wants to give those kinds of organisms greater scrutiny, to think through the potential problems more carefully.

I think above all, as a matter of public policy, what we ought to do is try to identify, with the help of the ecological community, what are the generic problems that are likely to occur, to the extent that there are generic problems in release of rather novel organisms, and then get some research started on these. We need to identify and design the kinds of fundamental experiments that were done so successfully in the context of the biohazard debate 7 or 8 years ago to get at some generic concerns, to try to identify what those experiments are and get on with them, so we do not have to analyze every organism that is out on the far end of the continuum on a case-by-case basis. We can expect to be able to define classes in designing these experiments and to gather data on those classes so we will be able to make decisions efficiently.

Mr. RIFKIN. I have to interject a disagreement, a very deep disagreement, as to what has just been said about continuum, looking at it in a regulatory fashion as if it is a continuum. Let me cite two examples to show the problems.

Back in 1980, General Electric went to the Supreme Court because they developed a micro-organism that eats up oilspills and they wanted to patent it. The problem with the Supreme Court was that we had not had any past experience under patent laws for patenting living things. The patent laws were not designed to include living things.

My organization provided an amicus curiae along with the Solicitor General's case. If you take a look at the proceedings and the battle between the amicuses and Justice Burger's decision, you see the beginning of a precedent for redefining the meaning of life which has long-term regulatory implications.

In order to squeeze living things into old patent laws, industry and many of the amicus briefs suggested that there is very little distinction between life and nonlife at the periphery, and further went on to say that living things are made out of two types of processes: physiochemical and vitalistic. Vitalistic is just a term we use before we have learned the physiochemical properties.

They said since all living things are made of chemicals and all chemicals in combination are patentable, therefore a living thing is patentable. I suggested at that time it is a new form of reductionism, by setting a long-term precedent by suggesting living things can be reduced to the chemical components that make them up.

Now, 4 years later, we see another problem popping up at EPA. EPA is attempting to assert jurisdiction over biotechnology products under TSCA. TSCA was designed for chemicals. So now EPA

is saying its statutory authority covers living things and living things can be for statutory purposes defined as chemicals.

Senator Durenberger, in the long run if we try and squeeze the biotechnical age into petrochemical systems, we are going to have problems in court systems, patent laws, in regulatory agencies, that are absolutely unparalleled, especially when we move to mammals and human beings, genetic engineering, genetic introductions and alterations and reductions.

What I am seeing is how a regulatory procedure very, very forcefully, if not subtly, begins to redefine our concept of life. What I am afraid of is the philosophical and social implications down the line when our children and their children grow up in a legal code which has reduced living things to the chemical properties that make them up. If that indeed comes about, the implications move well beyond the regulatory boundaries and move into the whole fabric of our social life.

Senator DURENBERGER. On that subject, and then I will ask you to respond also, Mr. Doyle, I would be curious to know what any of you know about how the insurance industry is reacting to genetic engineering, especially to the deliberate release of organisms.

Mr. DOYLE. I can't speak to the question of insurance right now, but I did want to respond to Dr. Jackson's remarks.

Senator DURENBERGER. Fine.

Mr. RIFKIN. I can speak very briefly about it. Getting back to the patenting of the micro-organism, I was curious after the Supreme Court decision on micro-organisms why General Electric didn't go ahead and use the micro-organism. On several occasions, one in particular, I asked Dr. Jack Abardy, who was the creator of this new form of life, why they had not used the micro-organism. I never did get a satisfactory answer.

Can I tell you what my speculation is without being able to ground it on any specific evidence? I don't think there was an insurance company in the country that would insure that micro-organism. I don't believe there was an insurance company anywhere in the world that wanted to take the risk of putting its insurance liability onto introducing that micro-organism into the environment.

That is speculation on my part, but from what I have heard over the years, there might be some basis for it.

Dr. JACKSON. I can also respond to the question on insurance, if you would like. Genex and other new biotechnology companies in the industry, so far as I am aware, have had no problem in getting liability insurance. We have normal policies and normal rates.

Mr. DOYLE. Senator, I would like to respond. I think one of the things that we are missing in this debate—I mean we hear an awful lot about this continuum of genetic technology from neolithic man up to the present day; that we have been massaging the genomes of crops for a long time, and that now with genetic engineering, there is no difference. But I think there is a very fundamental difference.

I think one of the differences is that we are doing this with our eyes open now. We can actually see the DNA and see the genes; and coupling that ability with other modern technology—such as the computer in the laboratory, which is going on today in advanced laboratories throughout the country—is an awesome power.

You are finding, for example, the ability to match genetic structures with chemical structures, as in herbicide resistance. And there is a whole new line of plant growth, regulators—new products coming out in that area.

My concern is that with this speed, you take an agency like EPA—assuming EPA gets a jurisdictional slice of this area—new products will be coming in, thousands of them, to the agency for review. With the new speed and capability of producing new products in such volume with this new technology, I wonder whether our agencies are going to be able to keep up with doing the toxicity evaluations that have to be done. I think it is clear, and I am sure this subcommittee knows, that the National Academy of Sciences just recently noted the fact that even with existing pesticides, we don't have adequate toxicity data for 66 percent of what is in use now. I think this technology—genetic engineering and biotechnology—does present us with a volume problem for some agencies like EPA, and the ability to evaluate.

Senator DURENBERGER. Dr. Jackson, you have the last word.

Dr. JACKSON. I would like to agree with Mr. Doyle. I think there is a volume problem here. The question is what do we do about it? Do we give the agencies, either the existing ones or some new one, the capability to deal with the volume problem or do we throw up our hands and say no, we can't do it, we are going to slow down or stop the progress? That I think is really the choice that we face.

To me, the sensible answer is to try to deal with the problems as the work is developing because there are so many benefits associated with it.

Senator DURENBERGER. That is the dilemma we have been dealing with in the subcommittee for 2 years and haven't found an answer.

Mr. DOYLE. I wanted to say one last thing. I think that funding is certainly necessary to be able to do toxicity evaluation and testing. But there are also some other kinds of approaches that can be taken. Take USDA, for example. We believe there are benign and very beneficial applications of this technology in the agricultural area. If USDA were to be given a mandate that said channel your biotechnological research dollars into finding out how you can lower the cost of production for farmers and protect the environment, we feel there may be a coupling there. But that kind of a mandate has to come from Congress. To direct biotechnology research in that kind of fashion would be, in our opinion, a very constructive thing to do with this technology.

Senator DURENBERGER. It would be extraordinary to have that kind of message come from Congress.

Thank you very much for your testimony. We may submit other questions to you in writing. We appreciate very much your willingness to testify on this subject. We will call on you again. Thank you.

[Whereupon, at 12 noon, the subcommittee was recessed, to reconvene subject to the call of the Chair.]

[Statements submitted for the record follow:]

Testimony of
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Hearings on
The Intentional Release of Genetically
Engineered Organisms

Subcommittee on Toxic Substances and Environmental Oversight
Committee on Environment and Public Works
United States Senate

September 27, 1984

Genetic engineering has emerged from the laboratory and entered the market. As the debate over the risks and benefits of laboratory research on new genetic engineering technologies came to an uneasy conclusion in the late 1970s, private firms rapidly began to translate the knowledge gained in the laboratories into commercially useful applications.

The very first commercial applications of recombinant DNA research have used genetically engineered micro-organisms in fermentation technologies to make useful pharmaceutical products. Similar commercial fermentation technologies may soon yield a whole host of other commercially useful products. While fermentation technologies raise some legitimate public health concerns, especially with respect to workers in fermentation plants, these concerns can be alleviated to a considerable extent through the same vehicles that reduced concerns over laboratory research -- physical and biological containment. Fermenters can be designed to be virtually leak-proof, and the organisms that are used in fermentation technologies can be engineered so that they cannot survive other than in special environments that do not exist in the natural environment. In addition, fermentation technologies can be closely supervised to ensure that the genetically engineered micro-organisms that produce commercialy useful products are killed when their job is done. By exercising relatively simple precautions, companies can ensure that the risks posed by fermentation technologies that use well-characterized recombinant DNA will not be appreciably greater than the risks of older fermentation technologies that do not use genetically engineered micro-organisms.

Genetically engineered micro-organisms can also be commercially useful in ways that require that they be introduced on a large-scale basis into the natural environment. I shall refer to these uses as "loarge-scale release biotechnologies."

For centuries, mining companies have used micro-organisms to leach valuable metals from low-grade ores. More recently, it has been suggested that genetically engineered micro-organisms could be useful in pollution control and tertiary oil recovery. Since the genetically engineered micro-organisms in these technologies must enter the environment in very large quantities, however, these micro-organisms are much harder to control than those used in fermentation technologies. Physical containment is generally impossible. Monitoring for the presence of the bugs in the environment is very difficult, and detecting any subtle effects on humans and the environment could be virtually impossible. Moreover, biological containment is not very useful as a protective device, because the usefulnes of the large-scale release technology depends upon the organisms surviving in the environment in which they are released.

Perhaps the most disturbing aspect of large scale release biotechnologies is the fact that the micro-organisms will proliforate, as soon as they have found a suitable niche. For example, if the recently reported genetically engineered micro-organism that may inhibit the natural frost formation process does in fact have a selective advantage over its natural cousin, then it could in time replace the cousin everywhere in the world. If at some later point in time we discover some unanticipated detrimental impacts of the technology, it may not be possible to call it back like we recall defective automobiles.

Finally, before we decide to employ large-scale release biotechnologies, we should carefully examine the possibility that a use of the technology that is beneficial to one person or group may be detrimental to another person or group. Our experience with weather modification technologies suggests that the benefits of a technology can also be its detriments. For

example, rain may be a boon for farmers but a bane for golfers. When the benefits of a technology are also costs, we need to examine that technology carefully to ensure that the benefits on the whole outweigh the costs. In addition, we might think about reducing the negative impact of a cost-beneficial technology by providing some sort of compensation mechanisms through which the "winners" can make the "losers" whole. Traditionally, state tort law has provided this mechanism, but it is always useful to consider the capacity for the common law to deal with freshly emerging technologies.

All of the foregoing considerations suggest that it would not be wise to leap into a rapid commercial implementation of large-scale release biotechnologies before we are confident that a legal and regulatory regime is in place that can adequately address any unanticipated detrimental effects of those technologies.

Nuclear power was once a bright new technology that offered great promise for the future. Heavily promoted by the federal government, that technology developed at a rapid pace, until the public assessed and debated its full socio-economic effects. In my opinion, a large part of the extremely negative reaction of some to nuclear power in recent years stems from the "go-go" spirit with which, during its early developmental phase, it was promoted with little or no regard to its downside risks. When the nuclear power debate blossomed anew in the late 1970s, the opponents of that technology drew upon both the deep sense of public betrayal which accompanied the Three Mile Island accident and the revelation that experts were consistently overly optimistic. A similar fate could await the newly emerging biotechnologies a decde from now if the health and environmental risks of those technologies are not soberly assessed, publicized and addressed in an adequate regulatory framework.

I. ELEMENTS OF AN ADEQUATE REGULATORY REGIME

While the current predictions concerning the hazards of newly emerging genetic technologies are admittedly quite speculative, caution suggests that we examine existing regultory mechanisms to see what regulatory responses might be available should our current risk estimates prove erroneous. Throughout this exercise, however, we should be sensitive to the needs of a growing and potentially beneficial technolgy to be free of unnecessary regulatory constraints.

A. Data Collecting and Monitoring

Perhaps the most important and least intrusive component of any mechanism for regulating human conduct is collecting information on the need for regulation. This data-gathering function is a continuous one, beginning at the time the technology is being developed and continuing throughout its application. At the very least a data-gathering mechanism should be capable of compiling a central registry of hosts, vectors, industrially useful genetic sequences, and products and by-products. A risk assessor will also need information on the extent to which humans and other important environmental entities are likely to come into contact with genetically engineered micro-organisms.

Ideally, companies would thoroughly test organisms with the potential for large-scale application in the laboratory and in limited natural settings before releasing them in large quantities into the environment. Even adequate testing, however, will not prevent the organisms from picking up a harmful trait in the environment or from manifesting an unforeseen trait once they find an ecological niche.

The data-gathering mechanism should also be able to monitor the actual application of biotechnologies in order to detect the improper presence of

micro-organisms. Monitoring large-scale relese technologies will be especially difficult, because in many instances there will be no geographical "places" where the organism should and should not be. The monitoring task will devolve to looking for the micro-organism in unexpected niches, such as the human gut. While I am certainly no expert in the field of biological monitoring, I suspect that a good deal of research is needed in this area before we can have any confidence in a company's claim that a large-scale release biotechnology has been confined to its appropriate "place."

Finally, a monitoring mechanism should be capable of detecting actual instances of human and environmental harm due to exposure to genetically engineered micro-organisms and their products and by-products. In addition to recording systematic and unplanned exposure, a thorough monitoring program should include periodic medical surveillance of exposed persons and periodic monitoring of the surrounding environment.

One general problem that will no doubt arise in agency attempts to acquire data from biotechnology companies is the issue of trade secrets. Companies will be reluctant to disclose information to the general public on the nature of the micro-organisms that they intend to use and market, because competitors might use this information to market competing products without having to undergo research and development expenditures. Preserving the competitive advantage of someone who has made a useful discovery can protect incentives to develop important new products.

One solution to the "trade secret" enigma is to allow agencies to collect commercially sensitive information, but prohibit them from releasing that information. However, this solution requires the public to place its entire trust in the agency's ability to assess the information and reach the

correct regulatory decisions. It also precludes the agency from thoroughly supporting its determinations when they are attacked by regulatees.

Perhaps the best solution to the trade secret problem is a balancing approach that weighs the public interest in disclosure of health and environment related information against the privte interest in nondisclosure. Since innovative micro-organisms can now be patented, however, the balance should probably weigh in favor of disclosure. If a firm elects to pursue the trade secret route rather than the patent route to protecting its market, it should be prepared to justify why members of the public should not have access to information relevant to their health and well-being.

B. Risk Assessment

An appropriate risk assessment of large-scale use of genetically engineered micro-organisms would include at least two kinds of analyses. First, genetically altered micro-organisms should be thoroughly chracterized. This characterization should include analyses of the structure of the organism's DNA, the ability of the altered organism to infect humans and other organisms, the pathogenicity of the organisms, and the possible by-products of the organism. If the organism could be infective, an estimate should be made of the probability that human or environmental exposure would be of sufficient duration and in sufficient concentrations to creae a potential for damage in the infected entity. Professor Martin Alexander has suggested a useful list of components of an adequate risk analysis for large-scale release biotechnologies. He would have the risk assessor examine the probabilities of the following five events:

1. Environmental Release
2. Survival
3. Growth
4. Contact with Receptive Environment
5. Deleterious Effect*

To this I would add that the full social consequences of deleterious effects should be factored into the risk assessment.

C. Regulatory Controls

At this early stage in the development of biotechnology, it is very difficult to speculate upon the sorts of regulatory controls that might be appropriate for keeping the risks within acceptable bounds. If risk assessments of large-scale release biotechnologies reveal the need for regulation, it may be advisable to examine some regulatory options available to policymakers.

My preliminary conclusion is that regulation of large-scale release biotechnologies should be implemented through a permitting mechanism under which no use of such a technology would be lawful without a permit from an appropriate regulatory agency. The entity requesting a permit would be required to sustain the burden of demonstrating that the technology would not cause unacceptable environmental effects. This would give the regulatory agency good information on the extent to which the technology is in use and it would place the burden of conducting the risk assessment or the proponent on the technology.

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* Dr. Martin Alexander, Spread of Organisms with Novel Genotypes, presented to the Seminar Series on Biotechnology and the Environment, conducted by th American Association for the Advancement of Science for the U.S. Environmental Protection Agency, May 17, 1983.

Given the huge uncertainties that surround prediction of the environmental effects of large-scale release biotechnologies and given the potential for vast environmental harm, I believe that this stringent regulatory device is proper. It must, however, be administered by an agency that can command the public trust. The Atomic Energy Commission and Nuclear Regulatory Commission experience demonstrates that if the agency lacks public trust, licensing proceedings can rapidly degrade into expensive and time consuming affairs that, in the end, resolve very little.

IV. CURRENTLY EXISTING REGULATORY REGIMES

Having drawn some preliminary conclusions about the elements of an adequate regulatory regime, it is now appropriate to measure existing regulatory structures against the ideal to determine whether any existing agency or combination of agencies has sufficient authority to implement an adequate reguatory program. If not, then it may be appropriate for Congress to consider a separate regulatory program aimed at the new biotechnologies. In making this assessment, I will focus primarily upon two statutes -- the Toxic Substances Control Act (TSCA) and Section 361 of the Public Health Service Act (PHSA).*

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* One predictable use of large-scale release biotechnologies is to mitigate or kill pests. If a substance or mixture of substances is intended to prevent, destroy, repel or mitigate a pest or to be used as a plant reglator, defoliant, or desicant, then it may not be sold, distributed or used until it is registered by the Environmental Protection Agency under the Federal Insecticide, Fungicide, and Rodenticide Act. This statute is precisely the sort of licensing statute that I have in mind for regulating large-scale release biotechnologies. Thus, for large-scale release biotechnologies that are pesticides, an adequately regulatory regime already exists. Recent problems with the data base for existing pesticides, however, might cause some concern about the ability of the Office of Pesticide Programs in that agency to command public trust. See EPA Pesticide Regulatory Program Study, Hearing before the Subcommittee on Department Operation, Research and Foreign Agricuture of the House Committee on Agriculture, 97th Cong., 2d Sess. (1982).

The Toxic Substances Control Act was enacted to provide a comprehensive mechanism for addressing the hazards to health and the environment of chemical substances. To date, however, EPA's implementation efforts have been slow and halting. Nevertheless, the statute is a large repository of regulatory power that EPA may draw upon when necessary.

TSCA regulates only chemical substances and mixtures. While TSCA is clearly an appropriate vehicle for regulating chemical products and by-products of biotechnologies, the ability of EPA to invoke the statute to protect the public from the risks that the micro-organisms themselves create depends upon whether the organisms come within the broad definition of "chemical substance." TSCA defines that term broadly to include

> any organic or inorganic substance of a particular molecular identity, including . . . any combination of such substances occurring in nature and any uncombined radical.

Although an entire micro-organism probably is not a "chemical substance," the DNA molecule within a genetically engineered micro-organism would seem to fit this statutory defi[illegible]. The molecule has a particular identity, even though that identity is not always ascertainable. Even if the combination of genes does not "occur in nature," the DNA might come within the definition of "mixture," which is defined as

> any combination of two or more chemical substances if the combination does not occur in nature and is not, in whole or in part, the result of a chemical reaction.

Clearly, this question is ripe for litigation if EPA decides to regulate the DNA of genetically engineered micro-organisms. If the courts refuse to find that the DNA is a chemical substance or a mixture, then TSCA will be largely unavailable to regulate industrial biotechnologies.

Section 361 of the Public Health Service Act gives the Food and Drug Administration (FDA) broad authority to promulgate regulations in

cooperation with the Centers for Disease Control (CDC) to prevent the introduction, transmission or spreed of communicable diseases. The Surgeon General of the Public Health Service may provide for inspection, fumigation, disinfection, sanitation and other measures necessary to carry out these rules.

A. Data Collecting and Monitoring

1. A Central Registry

As previously discussed, an essential element of a data collection and monitoring system is a central registry of hosts, vectors, industrially useful genetic sequences, products and byproducts. TSCA arguably gives EPA authority to require firms using genetically engineered micro-organisms to submit information necessary to compile an adequate registry, if the DNA in a micro-organism can be characterized as a "chemical substance" or "mixture." Under Section 5 of TSCA, the manufacturer of a new chemical substance must submit to EPA a notice of its intention to manufacture or process the substance. From this information, EPA could compile a registry of commercially useful genetic sequences. It is less clear, however, that section 5 would permit the agency to force companies to give it premanufacture notification of hosts and vectors, because they would not, under my reading of the statute, be considered chemical substances.

Should this application of section 5 of TSCA impose too great a burden on new biotechnology companies, section 5(h)(4) permits EPA to exempt the manufacture of any new chemical substance from all or part of the section 5 requirements if EPA determines that the substance will not present an unreasonable risk.

2. Surveillance of Technologies in Operation

Irrespective or whether EPA has authority to compile a central registry,

some agency should have the capability of gathering information on the potential risks of biotechnology by monitoring, conducting inspections nd requiring regulatees to keep accurate records. In addition, this surveillance function would be essential for the enforcement of any regulatory activity that the agency might undertake.

Section 8(a) of TSCA gives EPA blanket authority to require companies, other than small manufacturers, to maintain such records and submit such reports as EPA may reasonably require. This would appear to give EPA adequate authority to require firms to inform it of systematic employee and environmental exposure to genetically engeneered micro-organisms, their products and byproducts. In addition, EPA has authority under Section 8(a)(2)(E) to require manufacturers to submit existing health and environmental data, insofar as it is known or reasonably ascertainable. This authority could be used to provide EPA with existing studies on the survivability of host organisms, attempts to characterize genetically engineered micro-organisms, and risk assessments performed on these organisms.

Section 8(c) of TSCA independently requires manufacturers, processors and distributors of chemical substances to maintain records of "significant adverse reactions" to health or the environment alleged to have been caused by a substance, and section 8(e) requires immediate EPA notification by anyone who obtains information that "reasonably supports the conclusion" that a substance or mixture "presents a substantial risk of injury to health or the environment." These two provisions grant sufficient authority to require biotechnology firms to report diseases and other adverse effects caused by exposure to products and by-products of genetic technologies. Whether they give EPA the power to compel information about diseases that result from genetically engineered <u>organisms</u> depends upon whether it can be

said that the DNA (the chemical substance within those organisms) caused the disease.

Section 4 of TSCA allows EPA to order companies to conduct testing on chemical substances to determine their health and environmental effects if it determines that

(i) the manufacture, distribution, processing, or disposal may present an unreasonable risk; and
(ii) there are insufficient data to predict the substance's effects; and
(iii) testing is necessary to develop adequate data.

Under this section EPA could probably require testing for uncharacterized micro-organisms.

C. Risk Assessment

EPA has authority to use information that it acquires to assess the risks of newly emerging biotechnologies. Whether it can perform risk assessments as information becomes available depends upon wheter it develops and uses the data aggressively. Although EPA presently has little expertise in assessing microbiological risks, it is currently attempting to assemble such expertise in the Office of Toxic Substances. The Center for Disease Control is the nation's chief repository for determining the risks of infective organisms. An interagency effort might best accomplish a holistic assessment of all of the dangers posed by a particular large-scale release biotechnology.

D. Regulatory Controls

TSCA and the PHSA provide the administering agencies with a large arsenal of regulatory authority. If EPA determines that there is a "reasonable basis to conclude that the manufacture, processing, distribution, use or disposal" of a chemical substance will present an "unreasonable risk of injury to health or the environment," it may apply the

least burdensome of several requirements set forth in the statute.* In addition, if EPA has a reasonable basis to conclude that a particular manufacturer or processor is making a chemical substance or mixture in a manner that unintentionally creates an unreasonable risk, section 6(b) allows EPA to require the submission of quality control procedures. If EPA determines that those procedures are inadequate to prevent the substance from presenting an unreasonable risk, the agency may order the manufacturer to revise those procedures as necessary to remedy the inadequacy.

TSCA requires that the risk that a substance poses cross a designated threshold. The Administrator must have a "reasonable basis to conclude" that the substance will present an "unreasonable risk." The term "unreasonable risk" connotes a balancing process. Of course, for a newly emerging technology, both risks and benefits will be highly speculative, and EPA will probably be given great leeway in making this threshold determination.

Nevertheless, TSCA is not a permitting statute. The proponent of a technology does not have to apply to EPA for a permit to market that

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* EPA may apply:

(1) A requirement prohibiting the manufacture, processing, and distribution of the substance entirely or for a particular use.
(2) A requirement limiting the amount of the substance which may be manufactured, processed, and distributed.
(3) A labeling or warning requirement.
(4) A recordkeeping requirement.
(5) A monitoring requirement.
(6) A requirement prohibiting or otherwise regulating any manner or method of commercial use of the substance.
(7) A requirement prohibiting or otherwise regulating any manner or method of disposal of the substance.
(8) A requirement directing manufacturers or processors to give notice to the public and to distributors of such unreasonable risks and to replace or repurchase such substances as elected by the recipient of the notice.

technology. Unless EPA acts on the basis of information it receives under section 4 and 5 within a relatively brief period of time, the proponent of a technology may market that technology until such time as EPA can make the "unreasonable risk" threshold showing. The burden is on EPA to support the statutory finding. Given the large uncertainties that surround any attempt to assess the risks of large-scale release biotechnologies, this burden may be very difficult to meet in practice.

If the courts hold that genetically altered DNA in a host cell is not a "chemical substance," then section 361 of the PHSA is available to protect humans from communicable disease. Although this provision does not give FDA authority to regulate products and by-products, its unusually broad scope authorizes rules to protect humans from the risks of infection caused by genetic enginering micro-organisms. The courts have upheld broad interpretations of section 361 based primarily upon the asserted need to protect the public from exposure to contagious disease.

On the other hand, section 361 refers explicitly only to human beings. While damage to the environment often manifests itself in the form of public health problems, other ecological spoilage has only a tenuous link to public health. Arguably, however, once an agency has established "jurisdiction" over a substance, it should have authority under the National Environmental Policy Act to protect the environment as well. Furthermore, the Department of Agriculture might be able to protect non-human plants and animals by invoking the animal quarantine laws and the Federal Plant Pest Act. This statute is similar in structure and purpose to section 361.

The real problem of depending upon the PSHA to regulate biotechnology is that of resources. While the Public Health Service has a deep reservoir of expertise on communicable diseases, it is not really designed to prescribe

health and environmental standards or to license technologies. On the other hand, section 361 offers the greatest flexibility to select the most appropriate regulatory strategies for various genetic engineering technologies.

V. THE NEED FOR A SEPARATE STATUTE

The foregoing examination of statutory authority demonstrates that federal agencies probably have sufficient regulatory power to acquire information relevant to the risks posed by industrial use of genetic engineering technologies and to protect the public health and the environment if risk assessments demonstrate that regulation is necessary. The current statutory arsenal, however, is not without its weaknesses. Some of the most effective statutes, such as the Federal Insecticide, Fungicide, and Rodenticide Act, apply only to risks associated with the manufacture, distribution, and use of particular products. Other more comprehensive statutes -- the Clean Air Act, Clean Water Act, the Resource Conservation and Recovery Act, section 361 of the PHSA, and the Occupational Safety and Health Act, for example -- relate to particular risks. Only TSCA provides a comprehensive weapon that can target all risks and all stages of production.

The linchpin of a regulatory strategy that relies on TSCA is the validity of the assumption that the DNA in a micro-organism is a chemical substance or mixture. The argument for regulating micro-organisms through their DNA is convincing but risky. Hence, the only way to ensure adequate monitoring and regulation of the emerging biotechnologies may be to enact a statute that specifically addresses those technologies. A separate statute would give Congress or a state legislature the opportunity to craft reporting, testing, and regulatory requirements to the precise needs of the

new technology, rather than force an agency to attempt to fit the issues into an unsatisfactory statutory mold. By enacting new legislation, Congress also could choose the appropriate regulatory agency or create a new one. Because it would focus exclusively upon a single technology, the agency or subagency unit could rapidly acquire expertise in the technology and its risks. A new statute aimed at large-scale release technologies could adopt the permit approach, which minimizes the probability that harm-producing large-scale release biotechnologies will cause harm to the natural environment.

Strong arguments, however, oppose creating a new regulatory regime. Since the relevant technologies are new and rapidly evolving, disagreement undoubtedly will arise over what constitutes the approprite elements for the statute. A changing legislative problem is not alwsys conducive to intelligent draftsmanship. Although precedent abounds for aiming regulatory regimes at particular technologies -- for example, nuclear power and radio and television communications -- the technique has important disadvantages. The close interaction between the agency or subagency unit and the regulated industry could breed a familiarity that ultimately could mature into captivity. At the other extreme, the regulatory program, to justify its existence, might feel pressure to regulate unnecessarily. Finally, absent some crisis or other incident that brings the potential risks of new biotechnologies forcefully to the attention of the public, the issue probably will not generate enough enthusiasm to propel a bill through Congress.

Perhaps the most effective action that Congress could take at this juncture would be to amend the defintion of "chemical substance" in the Toxic Substances Control Act to eliminate any doubt that Congress intends for EPA to use TSCA's comprehensive regulatory process to regulate the risks posed by large-scale release biotechnologies.

Testimony to the Subcommittee on

Toxic Substances and Environmental Oversight of the Committee on

Environment and Public Works of the United States Senate on the Topic:

The Intentional Release of Genetically Engineered Organisms

Washington, D.C.

September 27, 1984

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The subject of the release of genetically engineered organisms into the environment, whether that release is intentional or inadvertent, has had a rather contentious history. In my view, some of the contention is legitimate in the sense that the contending parties are well informed as to the technical realities of the situation but simply come to different, honestly held conclusions regarding the likely outcome of the set actions, or simply disagree about what constitutes an acceptable degree of risk in a given situation. A significant amount of the contention is due to lack of understanding on the part of some of the contending parties regarding various technical issues. Finally, some of the contention is accompanied by the unmistakable sound of axes being ground in the background.

In my testimony, I wish to make several points which I believe are relevant to the release of genetically engineered organisms into the environment, and to what is the appropriate role of the federal government in regulating such releases. The first and most important point is that genetic engineering is a technology, not a new scientific discipline. It is a process, not an end result. It is possible to modify many organisms genetically using either conventional genetics or genetic engineering and to arrive at precisely the same result. It follows, therefore, that questions directed to the advisability of releasing an organism into the environment should be directed to the characteristics of the organism (including its genetic stability) and not to how the genetic characteristics of the organism were developed.

A second point which follows from the first is that a focus on whether only genetically engineered organisms required new federal regulatory mechanisms will almost certainly lead to bizarre, inconsistent, and indefensible regulation.

Indeed, it has already done so, as I shall explain below. A third point is that the environment or biosphere contains in it many mechanisms to keep it in balance. Some of these we understand and some we do not. However, it is in general (but not always) the case that most perturbations of the environment are resisted by these mechanisms, which tend to maintain whatever equilibrium has been established. Thus, in general (but not always), introduction of a new organism into the environment will be resisted by the mechanisms which maintain the environment in equilibrium. This will especially be the case if the organism has been genetically engineered to be a specialist at doing one particular thing well. Such specialization is not without cost to the organism, and it is a matter of experimental fact that most genetically engineered microorganisms survive very poorly in competition with naturally occurring microorganisms. This is not because they are genetically engineered per se but because the genetic engineers have tried to make them as efficiently specialized as possible for economic reasons, leaving them unfit to function well in any but the highly specialized environment of a fermentation medium. Microorganisms similarly modified using conventional genetic techniques have exactly the same problems competing in a natural environment.

Let me now elaborate on these points. Many people believe that an organism which has been modified by genetic engineering is somehow wholly different from normal organisms or variants of normal organisms obtained by conventional genetic mutation and selection or by breeding programs using conventional techniques. This is simply incorrect. It is true that it is possible to construct organisms using genetic engineering techniques which are modified in ways that would occur at most very infrequently in nature, but it is also possible to use these techniques as an alternative and more efficient means of constructing genetically

modified organisms which were previously constructed by conventional genetic techniques. In this latter case, it is perfectly possible that the two organisms which result from the modification by the two different sets of techniques will be literally identical. In such a case, it would be very difficult to argue that one organism should be regulated differently from the other simply because a particular set of techniques had been used to construct it.

It is useful to consider why so many people believe that genetic engineering confers some sort of special properties on an organism. There are, I believe, a series of reasons. The first is that not many people have taken a course in molecular genetics, and such a course is necessary to understand many of the technical realities of genetics and genetic engineering. The second is that our cultural heritage includes a large literature in which the process of genetic engineering in its broadest sense is assumed, either explicitly or implicitly, to confer special properties on the resulting organism. This literature goes back at least to Frankenstein, and includes more recent works such as Brave New World, The Andromeda Strain, The Boys From Brazil, and a large segment of contemporary science fiction. We thus are educated to a world view which, unfortunately, happens to be incorrect. The third reason I think we worry especially about genetic engineering was summed up most succinctly by Professor George Wald of Harvard who said "A living organism is forever." The notion is that mistakes in genetic engineering are likely to be particularly bad, because they are irreversible. However, this notion and its statement by Professor Wald, while attractively dramatic, does not fit the facts. Professor Wald is a distinquished scientist, but he cannot have been thinking about evolution, natural selection, survival of the fittest, extinction, and so forth when he said "A living organism is forever." We of course know that many hundreds

of thousands of species have become extinct during the course of evolution, by virtue of not being able to compete effectively in the natural environment. The vast majority of genetically engineered organisms are likely to share this inability to compete effectively, in large part because they have been designed with other purposes in mind.

The current controversy regarding field testing of so-called "ice-minus" bacteria can be used to illustrate another point made above: how focussing on whether an organism has been modified by genetic engineering rather than on what the properties of the organism are has resulted in policies which are logically inconsistent. Ice-minus bacteria are variants of either of two species of microorganisms, Pseudomonas syringae and Erwinia herbicola, which lack the ability of the parent microorganisms to promote the formation of ice crystals in supercooled water. The ice nucleation activity of the parent microorganisms is responsible for a substantial amount of the frost damage done to crops by temperatures in the range of 24° to 28°F. The ice-minus variants, which occur naturally or which can be produced by modifying the parent microorganisms using genetic engineering techniques, do not promote frost damage on plants they colonize. Moreover, if the ice-minus variants are sprayed on the plants at appropriate times, they are able to reduce the population size of the ice-nucleating parent microorganisms to the point that frost damage is substantially reduced. This information has been obtained from experiments using naturally occurring ice-minus variants in laboratories, greenhouses, and field trials. Experiments with genetically engineered ice-minus variants in laboratories and greenhouses have confirmed that these organisms behave in the same manner as the naturally occurring ice-minus variants. Field trials of the genetically engineered variants, however, have been the subject of much dispute and are presently prohibited.

The ostensible reason for prohibiting field trials of the genetically engineered ice-minus variants is that their effects are unknown and might be damaging to the environment. One is forced to conclude, however, that the real reason for prohibition is that the organisms are genetically engineered. As mentioned above, field trials with naturally occurring ice-minus variants have already been performed. So far as I am aware, there have been been no claims of any harmful effects arising from these field trials and there is no prohibition on repeating these trials with an organism which has been modified by conventional genetic techniques rather than by genetic engineering techniques. Situations as obviously inconsistent as this make for bad regulation. If ice-minus bacteria are harmful, they should not be placed in large quantities into the environment irrespective of how they are prepared. Similarly, if they are not harmful, the fact that they have been prepared using genetic engineering techniques is immaterial. Finally, it is worth noting that other biological techniques for reducing the damage caused by Pseudomonas syringae-promoted ice nucleation have also been developed. One such technique involves spraying crops with suspensions of bacterial viruses which grow on and kill Pseudomonas syringae. These naturally occurring viruses, in killing a whole population of bacteria, undoubtedly introduce an ecological perturbation, and probably a significantly larger one than the introduction of so-called ice-minus bacteria which differ from normal microorganisms by only one or a few genes. I wish to emphasize that I am not taking a position as to the relative safety or efficacy of the various biological approaches to dealing with crop damage promoted by ice-nucleating bacteria. What I am saying is that safety and efficacy should be the basis for regulatory action, not the mechanisms by which the organisms have been modified, unless those mechanisms can be demonstrated to affect safety and efficacy.

In order for regulation of products produced by biotechnology to achieve the desired result of safety in a manner that can be administered and defended as being logically consistent, it is important to recognize that there is not a genetic engineering or biotechnology industry *per se*. Rather, there are a large number of companies using new techniques of biotechnology, including, but by no means limited to, genetic engineering techniques, to make a wide and growing diversity of products. The vast majority of these products fall into categories currently regulated by FDA or EPA or USDA. In these categories, regulation is generally on the basis of the product's characteristics and the uses to which it is to be put, which is as it should be, and not on the basis of the technology used to produce the product. I see no reason why this present regulatory structure needs to be fundamentally altered for products produced in, containing, or consisting of genetically engineered organisms. Similarly, if such products are to be released into the environment, there is no reason I know of why the present regulatory structure is fundamentally inadequate to evaluate and appropriately regulate such releases.

This is not to say that present regulatory mechanisms or agencies are ideal or that they function as well as they might. For instance, if the EPA is going to be involved in regulating the release of products produced using genetic engineering, as would seem appropriate given its charter, then the agency will need more personnel who are familiar with this technology that it now has. The EPA will need to develop the same level of internal expertise with respect to genetically engineered organisms that the FDA has already done. To the agency's credit, I believe it recognizes this need and is moving to fill it. Because the agency is now drafting regulations which would apply to products made using genetically engineered organisms, and to release of such products into the

environment, it is important that these personnel be provided sooner rather than later. A similar need exists at USDA. The regulatory agencies are being asked to cope with a host of new products made possible by rapidly developing new technology. They need help to carry out their mission effectively.

In the short term such help can perhaps come in part from the Recombinant Advisory Committee (RAC). The RAC, the rest of NIH, the NSF, and the FDA are clearly the major loci of technical expertise in biotechnology in the federal government at the present time. However, except for FDA, these agencies are not regulatory agencies and lack the expertise in regulation which is just as important as technical expertise. Perhaps, at least as a temporary measure, an interagency group incorporating the RAC and supplemented by members from the major regulatory agencies which will have to deal with biotechnology, could serve both as a source of expertise on biotechnology and as a clearinghouse which would help advise the regulatory agencies in situations where jurisdictions may appear to overlap.

In concluding my testimony, I would like to make one more major point. There have been several calls for prevention of any deliberate release of genetically engineered microorganisms into the environment until we understand the ecological situation better and have a better predictive capability with regard to the outcome of the release. As a scientist, I must ask "Where is this better understanding and predictive capability going to come from?" The data upon which better predictions can be based must come from experiments. Science gains its better understanding of the world in which we live by doing experiments, and by definition the outcome of an experiment is not predictable in advance. A call for a ban on experiments in a particular field is a prescription for paralysis in that field. This does not mean that scientists or others have the right to perform any experiment at any time. It does mean that we as a society must accept some measure of risk in order to foster progress, and that we must not doom ourselves to stagnation and paralysis by chasing the unobtainable goal of a zero-risk world.

Testimony of Daniel Simberloff on potential ecological effects of releasing genetically engineered organisms, for hearing on "The Intentional Release of Genetically Engineered Organisms" by the Subcommittee on Toxic Substances and Environmental Oversight (Sen. Dave Durenberger, Chairman) of the Senate Committee on Environment and Public Works, September 27, 1984, Washington, D.C.

Daniel Simberloff
September 18, 1984

INTRODUCTION

I am an evolutionary ecologist, and among topics that I have studied are: 1) how ecological communities are organized, 2) the effects of introduced species on ecological communities, and 3) the ecological effects of genetic change (evolution) of native species on their communities.

The gist of my testimony is this: There is a popular misconception that ecological communities are stable, saturated entities, with all "ecological niches" filled, and no room for new organisms - either exotic species, introduced from other regions, or native species that have new genes. Furthermore, this view of nature suggests that communities are robustly organized, with each species held in check by its interactions with predators, parasites, pathogenic microorganisms, etc. A new organism would thus be unlikely to have much of an effect on a community: there would be few resources available to it, and it would not be adapted to deal with the host of enemies that it would encounter.

This view of a robustly balanced nature may be appealing and comforting to us, but it is incorrect. Ecologists have amassed evidence that communities are never full; there are always new ways to make a living if the right new species or new genotype of a native species comes along. Strong evidence for this assertion comes from studies of introduced species and of slightly changed native species. These two kinds of events - new species and new genotypes of native species - are not qualitatively different. In both instances, a community is faced with a novel biological entity. In both instances, the new element may not even be able to survive, and, if it does survive, it may not have a major impact on the existing components of the community. There have, however, been disastrous effects of both sorts of events, and a new genotype of an existing species may become a new species, even if the genetic change is initially very slight. Thus, the events are ends of a continuum, and should be considered together.

I contend that release of genetically engineered organisms into the environment is clearly part of this continuum. In fact, it is from an ecological standpoint exactly the same as when a new mutant occurs naturally to a native species. From the community's standpoint, it does not matter how the new genotype arose, just that

it now exists, and the community will have to deal with it in some way. Ecologists and evolutionary biologists possess sufficient expertise that, together with other specialists, they would be able to implement assessment and monitoring procedures that would minimize the possibility of ecological damage. Such procedures would have to be rigorous and time-consuming, but the potential for economic damage is so great in their absence that they should be instituted immediately.

GENETIC CHANGES IN NATIVE ORGANISMS, AND THEIR ECOLOGICAL EFFECTS

When an event happens in nature, as opposed to in a controlled experiment in the laboratory, it is always much more difficult to describe it with absolute assurance. Thus I cannot say, in any one of the examples that follow, that we can be completely certain that genetic change is the only cause for the subsequent ecological damage, or that we have described the nature of the genetic change fully. I can say, however, that in each example the evidence for the key role of genetic change is compelling, and that in some of these cases there has been sufficiently detailed genetic research to be certain that the genetics is a very large part of the story, if not the whole story.

The apple maggot, Rhagoletis pomonella, is a good example, studied in detail by Bush (1969, 1974). This fly is an economically important pest of apple, but was originally almost wholly restricted to a different plant, hawthorn. It was not even found on apple trees that were present with hawthorn. Then, suddenly, in 1865, it was reported attacking apples in the Hudson River Valley, and a little later in southern New England. From this focal point, the apple race, which may even qualify as a separate species, has spread to be found over the whole northeastern and central part of the U.S. Bush feels that the original host shift from hawthorn to apple rested on a single mutation, and that this kind of event may have occurred much more frequently in the history of life, and may account for the large number of closely related insect species that attack different host plants. The only thing that is special about this particular case is that there were sufficiently good records of the host shift, and the possibility of genetic analysis of many of the traits of this fly, so that it was possible to reconstruct what happened.

Another example, without a strong genetic analysis to support it, but with clear records of a sudden change in the geographic range of a species, is the collared dove, Streptopelia decaocto, a European and Asian bird originally restricted to the Balkans. It lived in parts of the Balkans for over 200 years and showed no inclination whatsoever to spread (Mayr 1963). Suddenly, at the end of the 1920's a few individuals were found in Hungary, then western Yugoslavia, then Austria, and now they are a pest all over western Europe. A similar expansion occurred in its Asian range (Nowak 1975). Not only was there no help from humans, but the expansion occurred in spite of tremendous hunting and other measures that slowed it down. Mayr suggests that a mutation is probably the reason, one that causes individuals not to home as strongly as they orginally had. He suggests a similar scenario for another European bird, the serin (Serinus canaria) that suddenly expanded its range, and there are other reports in the European literature for rapid range expansion of

a bird and a hamster in which a single genetic mutation is claimed to be the cause (Nowak 1975).

Southern maize leaf blight (Helminthosporium maydis), a fungus that devastated the corn crop in the southeastern U.S. in 1970, is another good candidate for swift genetic change. Since the 1940's corn breeders had been using cytoplasmic male sterility in the production of hybrid corn seed. The particular cytoplasm they used made the plant susceptible to the blight, yet the blight did not occur until 1970. The immediate cause of the epidemic has not been conclusively established (Vanderplank 1978), but it is known that favorable weather is an insufficient explanation and that there was a genetic change in the fungus itself from a race (O) that was not of much consequence to a race (T) that produces characteristic toxins and that causes different symptoms.

The rice brown planthopper (Nilaparvata lugens) is a major pest of rice in Asia, and the contribution of quick genetic change to its pest status has been thoroughly studied (Sogawa 1982). Until recently this insect was a minor problem, but in the early 1970's a severe infestation occurred in the experimental farms of the International Rice Research Institute in the Philippines. Not only did the planthopper itself cause damage, but it transmitted harmful viruses as well. The outbreak quickly spread to Indonesia, then to the Indian subcontinent. It has been established that the cause was genetic. In brief, rice has several sets of "resistance" genes that resist the effect of the insect, but, as quickly as these resistance genes spread through the rice population, "virulence" genes arise in the insect and overcome the resistance by the plant.

The Hessian fly (Mayetiola destructor) is originally from Europe, and so is not a native species in the U.S., but it has undergone genetic change in the U.S. that has made it a dangerous pest of wheat, and the way in which this change has come about is very similar to the scenario that I just sketched for the rice brown planthopper (Diehl and Bush 1984). There are complexes of resistance genes in wheat and virulence genes in the fly. Historically, what has happened is that resistance genes increase in frequency (lessening damage to the wheat crop), but virulence genes eventually increase in frequency in the fly and it becomes a problem again.

One can easily see that the examples of the rice brown planthopper and the Hessian fly are quite analogous to the well known problem of the development of pesticide resistance in many insects. Because pesticide resistance occurred so recently, and in so many economically important insects, and because the chemistry and mode of action of pesticides are usually well established, it is much easier to trace the genetic basis of pesticide resistance than it is to unravel the causes of sudden changes in species in nature. Resistant strains had evolved in 364 arthropod species by 1976, and these pests were resistant to at least 57 pesticides (Georghiou and Taylor 1976). The devastating ecological disruption, health effects, financial loss, and socioeconomic effects are well known, and are enumerated by Georghiou and Taylor (1976) and Sharples (1983), so that I need not repeat them here. I would like to elaborate on resistance, however, to show how a

small genetic change can lead to a dramatic change in a species' role and importance in an ecological community, and can even disrupt the structure and function of the entire community.

Many insects become resistant to pesticides by a very simple means. They have a sufficient number of genes in their populations, and they have a sufficiently high natural mutation rate, that they either have or quickly produce genes that confer resistance to almost all chemicals that humans can challenge them with. The pesticide itself becomes the agent of natural selection that causes the rapid evolution of resistance, as individuals that have resistance genes survive and reproduce at a higher rate than those that lack such genes. The frequency of the resistance genes thus increases, and after a number of generations of this process, the vast majority of individuals have these genes and are resistant.

The genes that confer resistance are of many different types. They can affect behavior - for example, they can cause insects to sit on the bottoms of leaves instead of the upper surface, and thus to avoid aerially dispersed pesticides. They can affect membrane permeability, so that the pesticide cannot reach the organ or tissue of the insect where it would act. Most often, the gene that confers resistance does so by causing a slight change in a biochemical pathway, rendering the pesticide less damaging. A target enzyme may change slightly, so it still performs the catalytic function that the insect requires, but is less sensitive to damage by the pesticide. An enzyme may be slightly modified so that it detoxifies the pesticide, by changing its chemical structure and rendering it innocuous. Although the exact means of resistance are many, they have usually been found to be due to single genes (Brown 1977). For example, DDT-resistance involves at least three mechanisms, each controlled by a single gene. Two of these mechanisms change the DDT molecule, and the third renders the insect's nerves less sensitive.

A resistant pest can wreak havoc with an agricultural or natural community. The most common way in which this comes about is that those predators and parasites that had helped to keep it under control are themselves greatly reduced in numbers by the same pesticide that selected for resistance in the pest. The predators and parasites do not usually themselves evolve resistance nearly as rapidly, largely because they are present originally in much lower numbers and therefore are much less likely to have the resistant genes present in their populations for natural selection to work on. Without predators and parasites, the resistant pests can increase in number many-fold, outcompeting non-resistant species, reducing the populations of plants that they specialize on, and generally disrupting the community. The devastation brought about by the development of resistance to organochlorine pesticides by the boll weevil (Anthonomus grandis) and the tobacco budworm (Heliothis zea) and boll worm (Heliothis virescens) in Texas are well chronicled (Sharples 1983). A less widely publicized effect is that resistant insect vectors spread disease. Thus resistance is a public health catastrophe (Pal 1976). Since diseases are among the natural forces that help to control species in natural communities, increased numbers of some disease vector can work to the severe disadvantage of those species

susceptible to the disease and to the advantage of species that are unaffected by the disease. So the effect of resistance on disease rates has ecological consequences.

To summarize this section: Changes in one or a few genes happen all the time to species in nature. Most of these naturally occurring mutations are of no ecological consequence, since they render the organism much less fit and natural selection weeds out the mutation (Mayr 1963). However, occasionally a naturally occurring mutation confers an advantage on the organisms that have it, by allowing them to use some kind of resource that they have not used before, or to survive against some kind of mortality factor that had previously killed them. The spread of such a mutation would occur under any circumstances, but sometimes it is accelerated by human activity. In any event, a species that had not been a pest may thus become a pest; it may even produce a new species (as when the maggot on hawthorn colonized apple). Part of what happens when a species becomes a pest is that it becomes much more numerous. Often it also expands its geographic range, and/or begins to use new resources and habitats. All of these events cause it to interact in different ways with the species in natural communities - it may devastate some of these species and aid others. The ecological effects can therefore be enormous. All of these possibilities have been realized in some instances - they are not just hypothetical.

ECOLOGICAL EFFECTS OF INTRODUCED SPECIES

Just as a genetic change in a native species presents a challenge to the ecological community, so does the introduction of a new species. Many introductions of new species have become classic ecological horror stories. Some of these - the gypsy moth, the Japanese beetle, the water hyacinth, the starling - are well-known to all Americans. Introduced pests such as these have obvious effects, but there are also subtle ways in which introduced species can have great ecological consequences. One example is the fungus *Endothia parasitica*, the chestnut blight (Sharples 1983). Asian chestnuts are little affected by this Asian species, and American species of *Endothia* are not major pests of the American chestnut (*Castanea dentata*) that harbors them. The Asian fungus, however, was so deadly to the American tree that it had killed almost all American chestnuts by 1950. Shugart and West (1977) attempted to model the changes in forest structure and function that occurred when the chestnut was suddenly removed. It was one of the most widespread of all Appalachian trees, and, by virtue of its vegetative reproduction, fast growth, and shade-tolerance, was probably important in aiding general forest recovery after disturbance. Though the number of trees does not change much after chestnut blight, the species composition and the functioning of the forest are greatly changed. Nutrient cycling in the forest floor, production rates, and gas exchange are all affected. These changes are in addition to the obvious consequences of removing a tree that was used by wildlife (especially for its nuts) and by the timber industry.

Most introduced species do not have such drastic effects, either subtle or apparent. Most of them, in fact, do not survive. There are

no valid statistics on the fraction of introduced species that survive, since most introductions are not recorded, whether they occur naturally (as when the cattle egret colonized the United States) or by human transport. Introductions are especially unlikely to be recorded when they are unsuccessful (that is, when the introduced species fails to survive for long). I have, however, surveyed 854 instances of species being introduced into new regions where the introduced species survived, and where there are sufficient records to attempt to see what happened (Simberloff 1981). The most striking result was that usually nothing dramatic happened. In 678 of these 854 cases the effect on the resident community was so slight that one could not point with assurance to a single consequence of the introduction. Part of this result is simply ignorance; without performing exhaustive experiments and taking massive field data on all species in the community, one cannot know for sure what effects the introduction had. However, it is possible to say in these 678 cases that there was no change major enough that casual and/or partial scientific examination by trained ecologists turned it up.

The remaining 176 introductions produced a variety of ecological changes in the ecological communities that received them. There were 71 extinctions of native species, most of these brought about by predation of the introduced species on a native species. Habitat destruction by the introduced species also often contributed to extinction of a native form. Many other effects occurred less frequently. For example, some native Hawaiian birds have been extinguished by diseases carried by introduced birds, such as poultry. In some instances this extinction by disease also required introduced insects, mosquitoes, to act as vectors. In addition to extinctions, there were a variety of less extreme effects caused by these introduced species - through habitat destruction, predation, competition, vectoring of disease, parasitism, and other means, they reduced populations of one or more native species and thus changed the structure of the community, sometimes substantially. A good summary of the community ecological effects of many introduced species was published by Elton (1958).

There do not appear to be any single traits that characterize those communities that are particularly subject to disruption from introductions, or those sorts of species that are especially likely to cause problems. Two kinds of ecological communities that seem particularly prone to damage from new species are agricultural communities and island communities, but there are many examples where both sorts of community do not suffer greatly from particular introductions, and there are also many examples where completely different sorts of communities <u>are</u> greatly affected. A careful examination of each case reveals idiosyncratic aspects of the biology of particular species, and of interactions between species, that determine whether a particular introduction will or will not cause damage. This is not to say that there is no way to predict what harmful effects an introduction might have. In retrospect, a careful ecological study of the native community and of the proposed introduced species would, in most instances, have revealed the danger that was later realized.

HOW TO MINIMIZE THE POTENTIAL FOR ECOLOGICAL DISRUPTION

Genetic engineering offers the promise of great benefits to humankind, especially in the areas of health, agriculture, and environmental management. Some introduced species have been very helpful to us. One need only think of tne many fruits and vegetables that are staple foods; most of them are not native to the Americas. Or one can consider the many millions of dollars that are saved each year by biological control - the use of introduced predators and parasites to control damaging insects. Similarly, new genotypes created by science have been of great benefit - plant and animal breeders have increased food production enormously by genetic manipulation.

But just as novel genotypes of native species and introduction of new species have at times caused staggering ecological problems, so are such disasters possible from the release of new genotypes produced by the most recent means of genetic engineering. Research is underway to increase the resistance of crop plants to insects and pathogens; to extend the range or increase the virulence of bacterial pathogens of insect pests; to extend the range of physical and chemical conditions that will allow plant growth; and to broaden the range of substrates that will support the growth of microorganisms. Many of the new genotypes that will be produced in pursuit of these goals will be completely different from anything that nature has already produced by natural means of mutations. Changes such as these may allow the engineered organism to escape from one form or another of natural limitation on population growth, habitat range, or geographic range, and thus to cause the sorts of ecological damage that I have discussed above for new genotypes of native species and for introduced species.

All this is <u>not</u> to say that the spectre of release of ecologically engineered organisms is so grim that it must be prevented. It <u>does</u> suggest, however, that there are potential dangers and that great caution is needed. Ecologists and evolutionary biologists possess sufficient expertise that, in concert with other specialists, they can design and implement assessment procedures that will minimize (though never completely eliminate) the likelihood that a particular release will lead to major ecological damage. Analogous procedures are already in use in, for example, the testing of new pharmaceuticals required by the F.D.A. or in the environmental impact statements mandated by the N.E.P.A. As in these cases, risk assessment will always have to be on a case by case basis. However, the following potential adverse effects should always be considered:

1) Evolutionary

   a) Likelihood and nature of host range shifts.
   b) Likelihood of unregulated propagation.
   c) Likelihood of changes in virulence of parasites and pathogens.

2) Ecological

   a) Effects on competitors.

b) Effects on prey, host, and symbiotic species.
c) Effects of predators, pathogens, and parasites.
d) Role of new organism as vector of pathogens.
e) Effects on ecosystem processes, such as cycling of biogeochemicals.
f) Effects on habitat.

Finally, the release should be followed by a continuous process of monitoring for changes in the released organism and the community. A sufficient commitment of economic and human resources to a program of this sort would prevent some ecological crises that will almost certainly develop in its absence, and will minimize the possibility of unexpected problems. Whenever a self-reproducing entity, such as a genetically engineered organism, is released into nature, the difficulty of subsequent control once we learn we have made a mistake is so great that the most stringent pre-release safeguards are warranted.

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ENVIRONMENTAL POLICY INSTITUTE

TESTIMONY OF JACK DOYLE
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BEFORE THE SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT OF THE U.S. SENATE COMMITTEE ON ENVIRONMENTAL AND PUBLIC WORKS

THE INTENTIONAL RELEASE OF GENETICALLY ENGINEERED ORGANISMS

27 September 1984

Mr. Chairman, Members of the the Subcommittee:

For the record, my name is Jack Doyle. I am Director of the Agricultural Resources Project for the Environmental Policy Institute (EPI), a non-profit, public interest organization engaged in research, public education, litigation and lobbying. EPI works on energy, environmental and natural resource policy at the local, state and national levels. We appreciate the opportunity to appear before this subcommittee today to share our views on the very important topic of releasing genetically altered substances into the environment. We commend the chairman and the members of this subcommittee for initiating these hearings, and trust that they are only the Senate's first step into a careful and comprehensive examination of biotechnology and genetic engineering and how these technologies will affect society and the environment.

During the last three years at EPI I have been working on a book about some of the changes our society, our nation's food and farm system, and our environment will likely experience with the application of biotechnology and genetic engineering to agricultural production. In the course of writing this book -- which is scheduled for publication early next year -- I have visited with numerous scientists and businessmen in the seed industry, at new biotechnology companies and at established corporations.

My discoveries so far leave the distinct impression that there is much promise for agriculture and the environment with the use of new genetic technologies. However, there are also some clear reasons for concern and caution.

Advances and breakthroughs in the science of biotechnology and genetic engineering have occurred much faster than anyone anticipated, even as recently as 5 years ago. Huge sums of capital are being invested in the U.S. and other countries, and a race has ensued among scientists, new biotechnology companies, major corporations and even nation states seeking technological supremacy in world markets. Now in the United States, as genetically-altered products draw nearer to commercialization, there is great pressure to secure swift federal approval for these products. Yet, outside of the House Science and Technology Subcommittee on Investigations and Oversight, there has been little public debate or policy forethought on the environmental or potential social consequences of this new technology. On the

environmental question, only a very few reports exist so far, among them, one prepared by the staff of the House Science and Technology Subcommittee on Investigations and Oversight in February 1984, titled, "The Environmental Implications of Genetic Engineering." Policy-making on the question of environmental release seems to be evolving more in the courts than it is in the Congress. But there are potential environmental ramifications with genetic engineering that need to be debated in the Congress; potential effects which need to be weighed very carefully before the federal government commits itself in any one direction.

In the genetic realm alone, there is every reason to be careful and cautious, and to question iron-clad assurances that genetic engineering is so exact and precise that everything is under control and there's nothing to worry about. We've heard that before. As recently as 1970, plant scientists generally thought that the genetic traits that determine disease resistance and/or susceptibility in crops were contained in the nucleus of the cell. But after the Southern Corn Leaf Blight wiped out 15% of the nation's corn crop in 1970, they discovered otherwise. They discovered that cytoplasm -- the liquid material contained in every cell -- also had something to do with the genetics of disease reaction. That was new information.

Today, as in 1970, we continue to learn new things about genes and how they act. Only in 1983 did we first hear the term "promiscuous DNA," meaning that DNA sequences could move about within the confines of the cell, in this case between

chloroplasts and mitochondria. Scientists studying this transfer activity at Duke University and the Carnegie Institution of Washington conclude that it is not a rare event, but a "general phenomenon." Before this discovery, scientists had assumed that intra-cellular organelles like chloroplasts and mitochondria were independent of each other.* Now they know differently, but how the DNA gets from one organelle to another is still a mystery.

While the movement of genes between chloroplast and mitochondria is a new discovery, the knowledge of mobile genetic elements is not. But sometimes, it has taken the scientific community a good while to accept such knowledge. In 1951, to the disbelief of her scientific peers, Nobel prize winner Barbara McClintock first offered her discovery of "jumping genes." McClintock discovered that the genes on chromosomes -- once believed to be stationary and therefore predictable in the genetic characteristics they controlled -- could move or "jump" from one chromosome strand to another, thus affecting changes in the expression of certain traits. What is most interesting and instructive about the McClintock episode is that it took nearly 20 years for the scientific community to finally accept her discovery.

What we may be dealing with in the inner genetic world of the cell is a system of interactions and adaptations somewhat

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*See, for example, Roger Lewin, "No Genome Barriers to Promiscuous DNA," Science, 1 June 1984.

akin to ecological systems of the outside world. That is, there may be an "ecology of genes" inside of cells and organelles which operates by principles similar to those of larger-world ecosystems. What is troublesome about genetic engineering in such a context is: (1) that these two worlds interact regularly, and (2) that one small genetic change in an organism might have large consequences, magnified many times throughout the environment.

On this last point, the available evidence seems to indicate -- based on the past introduction of exotic species into new environments, the low rate of survivability of alien organisms in new environments, and ecological principles of competition and predation generally -- that most genetically-altered organisms will not survive, but some will, and a few may create problems.* But we have no way of knowing which ones might cause problems because we lack what is called a "predictive ecology." We especially lack a predictive ecology in microbiology, and there is generally not good interaction between molecular biologists and ecologists. Further, the science of ecology is young and the few scientists who ply this field deal primarily with the ecological give-and-take of organisms in natural ecosystems, operating under natural rates of mutation and adaptation. Rapid,

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*See, for example, "Environmental Implications of Genetic Engineering," Hearing Before the Subcommittee on Investigations and Oversight and the Subcommittee on Science, Research and Technology of the Committee on Science and Technology, U.S. House of Representatives, 98th Congress, June 22, 1983.

man-made genetic changes introduced into these systems by way of gene splicing introduce a new variable, one that will, without question, revolutionize the way we think about ecology. Even the newest textbooks will need to be rewritten.

On the one hand, we have a science of ecology that is young, not yet "predictive"; on the other, we have a bustling new industry ready with genetically-altered microbes and other substances to be released into the environment. Now we are faced with the question of whether and how government should supervise such commercial activities. In our opinion, it is not a question of whether government should regulate, but how. To do otherwise would be to make the federal government an accomplice in an ecological crapshoot.

It is clear that a careful debate is necessary about how to regulate responsibly; one that covers all options and possibilities; and one that allays public fears and instills confidence that the new genetically-created substances for agriculture, mining, enhanced oil recovery, industrial bioprocessing and other uses will indeed be safe. While fostering scientific and technological innovation are important to our country, so are public health and safety and environmental protection.

But as the regulatory debate moves forward, these are some steps that can be taken. One is a badly needed infusion of federal research dollars for EPA, USDA, FDA, and the land grant universities to insure that we have a predictive ecology in place

before new genetically-altered substances are released into the environment. Moreover, federal funds earmarked for biotechnological research might build in a predictive or consequences requirement as a part of all such grants, which would serve the purpose of inculcating such forethought into the process at the same the research is being done. The quicker such measures are taken, the sooner biotechnology products can be introduced into the environment with some public confidence.

Our concerns for environmental safety and ecological impacts go beyond establishing a sound predictive science base and a responsible regulatory framework. Our concerns include the "potential secondary impacts," the indirect environmental and agricutural consequences of biotechnology -- such as how biotechnology may exacerbate the unresolved problem of pesticide safety; how supercrops or supermicrobes may affect the use of natural resources or the operation of major natural cycles such as the nitrogen cycle; how biotechnology's expanding use of microbes (some of which may become pathogenic to plants) in the processing of industrial products might endanger agricultural crops; and how the new products of biotechnology will affect the structure and operation of our nation's family farm system.

When we make genetic changes in crops, livestock and microbes, we need to ask very broad questions about their potential environmental and economic impact. If we genetically alter microbes that move about in the nitrogen cycle, for example, we must determine what those changes will do to the

balance of that system's operation as a whole. If we increase photosynthetic efficiency in crops by way of genetic engineering, will we raise other demands for water and nutrients? If we engineer and use plant pathogens in certain large scale industrial processes to make everything from xantham gum to industrial enzymes, we may increase the risk that such organisms could escape into agricultural environments where thousand-acre monocultures invite widespread crop damage?*

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*Today, there are at least a dozen known kinds of bacterial and fungal microorganisms being used to produce a variety of industrial products and fermented foods -- all of which are capable of producing strains that are pathogenic to crops. With the aid of biotechnology and genetic engineering techniques, the number of microbial projects for producing all kinds of commercial products and intermediaries for industrial processes is expected to increase significantly.

"Because of the increasing industrial use of plant pathogens," wrote a team of British scientists investigating biotechnology for the EEC, "it is important that European biotechnologists are aware of which organisms might be pathogenic for European plants. It might be expected that this should already be the case, but our experience in gathering information for this report has convinced us that it is not so." Indeed, these scientists found experienced biotechnologists unaware that particular organisms they were using or considering were pathogenic species. And that's not all.

"Just as we discovered biotechnologists unaware that some of the organisms with which they were concerned belonged to pathogenic groups," wrote the scientists, "so we found experienced plant pathologists unaware of current industrial uses of such organisms." As a remedy to this situation, the British scientists recommended that two lists be prepared: one comprising fungi and bacteria that could cause major damage to crop plants, a second list of current industrial uses of such organisms. Yet as of this writing, it is unclear whether either of these lists have ever been prepared for the EEC, or whether comparable lists exist for the United States. See C.G.T. Evans, T.F. Preece and K. Sargeant, "Microbial Plant Pathogens: Natural Spread, and Possible Risks In Their Industrial Use," A study of the necessity, content and management principles of a possible Community Action, Commission of the European Communities, XII/1059/81-EN., 74 pp.

However, we are most concerned that some developments in biotechnology and genetic engineering might foster an increase in the use of certain synthetic pesticides and perhaps exacerbate some environmental and toxic substances problems with which this subcommittee is well acquainted. In this regard, the genetic alteration of agricultural crops to make them withstand the deleterious effects of herbicides is an instructive example.

Herbicides are chemicals designed to kill plants. However, some crops have the natural ability to live with some herbicides; most do not. Wheat has an enzyme which detoxifies the killing action of Du Pont's new herbicide Glean. Corn produces an enzyme which makes it resistant to the lethal effects of the herbicide atrazine. Yet, soybeans and alfalfa -- two crops that might be used in rotation with corn -- are not tolerant to atrazine. Similarly, sunflowers, sugarbeets and lentils -- crops that might rotate with wheat -- are damaged by the herbicide Glean. Moreover, these crops can be damaged by these herbicides even when the chemicals are "carried over" in the soil from previous applications.

But that's where biotechnology and genetic engineering enter the picture.* Today scientists use tissue culture techniques in

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*See, for example, Jean L. Marx, "Plants' Resistance to Herbicide Pinpointed," Science, 1 April 1983; "The Hat market in herbicides," Chemical Week, 7 July 1982; and "Herbicides follow the current trend to low-till farming," Chemical Week, 9 May 1984.

the lab to screen thousands of cells for potential herbicide-resistant "survivors." For example, Monsanto's Plant Sciences Research Director, Robert J. Kaufman, testifying before a House subcommittee in June 1982, explained his company's work with alfalfa plants and the herbicide Roundup. "Alfalfa tissue was placed into culture first on solid media and later into liquid culture. In liquid culture, the cells were exposed to a lethal dose of the herbicide Roundup and the survivors were plated out for regeneration into whole plants. These new plants (or variants) were transplanted into the field and treated with Roundup the way a farmer would use the herbicide. Several variants were found to have field resistance to the herbicide."

One recent biotechnology company's prospectus, for example, it is noted that some U.S. scientists working with tissue culture techniques have screened and selected out plant cells to regenerate plants with resistance to the herbicide 2, 4-D, paraquat, and picloram (Tordon). In a few cases, scientists have also cloned genes for herbicide resistance that might be moved into plants that don't have that resistance now. Such matching of herbicides and plants genetically-altered to withstand them will increase the use of chemicals. We believe that this kind of genetic research and product development will create public health and environmental problems by <u>increasing</u> the load of herbicides in the environment. Attached to this testimony is a

sample list of companies now using biotechnology techniques and genetic engineering to incorporate herbicide resistance into new crop varieties.

Not much is known about the long-term effect of herbicides in the environment. Although current herbicides are generally not regarded to be as toxic as the chlorinated hydrocarbon insecticides used in the 1960s, they do have side effects. Not much is known about how herbicides completely break down, and according to some scientists, such information is only known for about 4 of the 150 herbicide compounds presently in use.* Herbicides such as atrazine have been found to cause chromosome breakage and other aberrations in plants. In fact, triazines -- the chemical family to which atrazine belongs -- generally are known to be mutagenic to some insects such as fruit flies. Moreover, recent revelations about one popular Monsanto herbicide, Lasso, found in Ohio drinking water, have raised new

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*See, for example, D.D. Kaufman and P.C. Kearney, "Microbial Transformations in the Soil," in L.J. Audus (ed.), Herbicides, Academic Press, 1976, pp. 29-64.

questions about herbicide safety.* Nevertheless, huge R & D investments continue to be made in herbicide chemistry, some of which is now buoyed by the prospect of genetic engineering.

Herbicide-resistant crops are but one area in a whole new world of agricultural chemistry that biotechnology may create. Research directors at many of today's leading chemical and pharmaceutical companies will tell you that they see a much more sophisticated era of agricultural chemistry ahead -- one that

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*In June 1984, Pesticide and Toxic Chemical News reported that EPA might cancel the registration of Lasso because of the discovery of minute traces of the herbicide in Ohio drinking water, which suggested that not all of the pesticide dissolves, as previously claimed. In reaction to that report, Leslie C. Ravity, a prominent Wall Street analyst for Saloman Brothers, withdrew his recommendation for the company's stock, causing a temporary panic in selling. On June 7th, the New York Stock Exchange halted trading in Monsanto stock for one hour due to the imbalance in orders. The stock dropped $1.50/share for the day.

Later reports about the possible EPA review of alachlor, the active ingredient in Lasso, cited links to cancer in laboratory animals. Lifetime feeding studies with technical grade Alachlor in mice and rats suggest that the material is capable of causing tumors in these laboratory animals when it is fed to them in extremely high levels on a daily basis for the greater part of their lifetimes, which is not representative of exposure for humans. The feeding levels in these laboratory animal studies were many thousand times higher than potential human exposure.

In reaction to the possible EPA review, Monsanto's Will D. Carpenter explained: "There is no evidence that Alachlor produces tumors in humans. The risks will be compared by the EPA with the benefits from Lasso," he said. "Lasso effectively controls weeds in major crops including corn and soybeans, increasing crop yield and quality. It is of major economic importance to U.S. agriculture.

"These benefits are known to millions of farmers and documented in economic analyses. The product is being used safely with no unreasonable risks. Any special review, if held, would confirm these results and uphold the product's continued registration."

includes plant growth regulators,* encapsulated and synthetic seed, new kinds of microbial pesticides, viruses, and genetically-enhanced bacteria. Who will decide whether these products are safe, economical and efficient in fostering agricultural production? Will they be ecologically sound? And how will the market sort out which ones are truly beneficial and productive?

Further, assuming EPA has jurisdiction over many of these new products, what will happen to the agency -- already overloaded with conventional pesticide analysis -- when thousands of genetically-altered products come before it for approval? We know that existing toxicity data on pesticides already in the environment are inadequate. The National Research

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*While some plant growth regulators may be beneficial and harmless in the environment, others may not be so benign. In July 1984, the U.S. Environmental Protection Agency announced a special review of Uniroyal's growth regulator ALAR, a chemical spray used on apples to retard ripening. ALAR also makes apples redder in color and increases their shelf life by 2-to-3 months. Used in orchards, the spray allows growers to extend the harvest season, employing fewer pickers over a longer harvest. Used on peanut crops in the field, the same chemical stimulates upright growth in the plant, facilitating harvest.

EPA initiated review of this growth regulator because it feared the substance could pose a dietary cancer risk in humans consuming raw and processed foods treated with the chemical. "The order of magnitude of risk from this chemical," said EPA pesticide official Michael Branagan in July 1984, "is similar to that of EDB." EPA initiated the review for the chemical when it discovered in tests on laboratory animals that daminozide, the chemical's name, caused tumors of the uterus, liver, kidney, lungs and blood vessels. Uniroyal officials, however, insist that the chemical is safe. "We don't believe ALAR poses a threat to either the environment or individuals," said James Sylie, Uniroyal's manager of crop protection chemicals. The results of EPA's review will not be known until 1986. Meanwhile, ALAR continues to be used.

Council recently reported that available data were insufficient to allow even a partial health assessment for some 66 percent of pesticide ingredients.* How can we insure that biotechnology will not spawn still more agricultural chemicals for which little environmental or toxicity data exist?

Could product research priorities in major corporations and universities emphasize lines of research that are more environmentally benign to begin with? Some commercial scientists have told me, for example, that the reason they are pursuing herbicide resistance in crops is because it is easy -- a single-gene change in some crops and one of the early gains of genetic technology. "You have to start with what's there to demonstrate what can be done," one researcher told me. It is an understanding, he said, that will lead to other more sophisticated breakthroughs later. Yet, herbicide-resistant crop varieties will be commercial products, and it is commercial products that this new industry wants most to show its stockholders, its underwriters, Wall Street and the media. While producing such products may be an innocent and necessary step along the path of genetic science, it will also be a highly capitalized step backed by a mass production system that insures a return on investment.

Our concern here is with momentum -- the commercial and scientific momentum that builds around any new and dynamic

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*Philip M. Boffey, "Few Chemicals Tested for Hazards, Report Finds," The New York Times, 3 March 1984.

technology. Our concern is that a certain kind of product momentum will be set in motion in the earliest stages of this technology that may be difficult to turn around should something go wrong; difficult to reverse because of huge capital investments, scientific careers on the line, and accrued political support. This momentum is building now on Wall Street, here in Washington, and in research laboratories across the country, and it will shape our agricultural system and the quality of our environment.

One measure of this momentum now building in U.S. agriculture, at least partially instigated by the business expectations for biotechnology, is the shift in the ownership of seed companies from family-owned businesses to corporate-held subsidiaries. The name of the game now, in what is rapidly becoming the agricultural genetics industry, is genes and expertise, and seed companies with plant germplasm on hand and plant breeding programs are being snapped up like nobody's business. We have documented well over 100 such transactions since 1968, and that is probably a conservative estimate (see attached chart). In the last 4 years alone, there have been at least 50 such transactions, with major corporations such as AMFAC, Anheuser-Busch, Atlantic Richfield, Cargill, Celanese, Lubrizol, Monsanto, Rohm & Haas, Royal Dutch Shell, Pfizer, Stauffer Chemical, and Upjohn all venturing into the seed business. Many of these and other corporations have also formed their own in-house agricultural biotechnology research efforts,

or have research contracts with university scientists. Some have also bought into biotechnology companies (see attached chart). Most biotechnology companies and major corporations working toward new agricultural genetics products are also moving very aggressively in the patent area -- patenting seeds, genes, and biotechnological processes. Biotechnology, in other words, is encouraging a new kind of economic configuration in agriculture and one that may eventually raise questions of cost for farmers and price for consumers.

With biotechnology we will be moving to a time when the alteration of the genomes of agriculture will result in an alteration of systems of agriculture. Just as we are now paying attention to the potential ecological consequences of genetic engineering, we must also plan for the social and economic changes that could come to agriculture and rural America with this revolutionary technology. For example, a genetically manufactured bovine growth hormone enabling cows to produce 40% more milk on less feed could have dramatic impacts on the dairy industry. Some estimates have suggested that if widely used, bovine growth hormone could result in a reduction of the nation's dairy herd by one-third. That would mean a dramatic reduction in farmers and farm numbers. A similar development in the beef or pork industries would not only affect cattle ranchers and hog farmers, but also feed grain producers nationwide. These changes, in turn, might lead to substantial change in federal farm policy.

To summarize, the Environmental Policy Institute finds that there are benefits and opportunities to come with biotechnology and genetic engineering in agriculture. There are constructive applications and inventions that can help to eliminate or reduce the use of chemicals in the environment, and these should be pursued sooner rather than later. There should also be opportunities to diversify our agricultural production base through the use of new kinds of crops and ways to reduce the farmer's cost of production with disease-resistant crops and the development of hardier crops. However, we also believe that there is need for great caution in the microbial realm, and that federal regulation and funding for predictive ecology research are both in order. Indirect and secondary impacts, such as those possibly resulting from the development of herbicide-resistant crops, should also be considered. Moreover, there is some need to examine the consequences of the potential corporate domination of the genetic substances that will control the growth of crops and livestock, and thereby the production of food.

Another important issue is the erosion of science in the public sector, now occurring in agricultural microbiology and agricultural genetics. We believe that there is a need to keep public sector science strong and independent of commercial goals so that alternatives are always being freely pursued.

We expect that many of these concerns will be addressed in the next Congress, and we urge this committee to continue then what it has started this week.

Thank you for the opportunity to express our views here today.

Appendices A through E follow.

ENVIRONMENTAL POLICY INSTITUTE

Appendices to Accompany the Testimony of Jack Doyle
Director, Agricultural Resources Project
Environmental Policy Institute

Before the Subcommittee on Toxic Substances and Environmental Oversight of the U.S. Senate Committee on Environment and Public Works

27 September 1984

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Appendix A

U.S. BIOTECHNOLOGY COMPANIES & CORPORATIONS WORKING ON HERBICIDE-RESISTANCE IN AGRICULTURAL CROPS

Company	Research Project	Approximate Date of Action or Notice of Research
Advanced Genetic Sciences, Inc. Greenwich, CT	AGS scientists recently succeeded in isolating tobacco mutants resistant to various herbicides by screening protoplast-derived colonies, and will be extending this project to other crops, including potatoes and rapeseed.	June 1983
BioTechnica International, Inc. Cambridge, MA	working to develop a vegetable variety that will withstand "less selective" herbicides	1983
Calgene, Inc. Davis, CA	has produced a gene that is resistant to glyphosate (a popular herbicide produced by Monsanto called Roundup), and is also working to develop crop varieties resistant to the herbicide phenmedipham (Betanal).	Nov. 1982
----------	has research contract with Kemira Oy (Finland) to develop herbicide resistant varieties of turnip rape	Nov. 1983

----------	has joint research program with Nestle S.A (Switzerland) subsidiary Nestec to develop herbicide-tolerant varieties of soybean	April 1984
----------	has research contract with Rhone-Poulenc Agrochimie (France) to develop new varieties of sunflower tolerant to the herbicide Bromoxynie	June 1984
DNA Plant Technology Corp. Cinnaminson, NJ	plans to conduct recombinant DNA work using extranuclear genes to introduce herbicide tolerance into new plant breeding lines.	1984
E.I. du Pont de Nemours & Co. Wilmington, DE	has cloned a gene that is resistant to the company's herbicide Glean and has developed tobacco plants with resistance to Glean 100 times greater than normal	1984
Molecular Genetics, Inc. Minnetonka, MN	has research contract with American Cyananid (NJ) to develop herbicide-resistant hybrid corn varieties	
Monsanto St. Louis, MO	working on herbicide resistance in a range of crops	1983
Rohm & Haas Philadelphia, PA	working to develop rice varieties resistant to herbicides	1984

Shell Development Co. Biological Sciences Research Center Modesto, CA	studying the genetic mechanics of herbicide resistance in plants generally; looking to find a gene in corn that would resist new herbicide Cinch (Cinmethylin).	1984

Note: This compilation of biotechnology companies and major corporations involved in herbicide-resistance work is a representative listing of such research now underway. Other companies are also involved.

Source: Compiled by the Environmental Policy Institute, Washington, D.C. from chemical industry publications, corporate prospectuses and reports, and conversations with industry officials.

Appendix B

MICROBES THAT CAN BE USED IN INDUSTRIAL BIOPROCESSING
AND/OR BIOTECHNOLOGY WHICH CAN BE PATHOGENIC TO AGRICULTURAL CROPS

NAME OF ORGANISM	KIND	PLANTS AFFECTED OR HISTORICAL INCIDENT	RECENT CROP DAMAGE IN U.S. (1977)	EXISTING OR POTENTIAL USES IN BIOTECHNOLOGY
Fusarium solani	fungus	has caused great problems in the Dutch cucumber trade		
Xanthomonas campestris	bacterium	causes leaf spot of alfalfa; common blight of beans; black arm of cotton;	$1 million (crucifers)	restriction enzymes xanthan gum production
Pseudomonas syringae	bacterium	beans	$8 million (all crops)	
Erwinia chrysanthemi	bacterium		$2.3 million (tobacco)	production of anti-leukemia enzyme
Erwinia amylovora	bacterium			capable of producing polysaccharide material
Fusarium graminearum	fungus	causes scab in cereal crops; hit Wales in 1942; also causes problems in rice & corn in Tropics		used to make single-cell protein; could be used to transform steroids
Agrobacterium tumefaciens	bacterium		$2 million (all crops)	used as recombinant DNA vector in some plants; could produce cytokinins for plant growth regulation
Endothia parasitica	fungus	destroyed Chestnut trees of eastern U.S.		used to make rennin
Sclerotium Sclerotinia Stromatinia	fungi	attack stems and tubers of various crop plants		used to produced scleroglucan gum; as "Polytran" by Ceca, S.A. (French Co.)

Pseudomonas marginalis	bacterium			could be used to produce enzymes for paper making
Corynebacterium fascians	bacterium			could be used to produce cytokinins, chemicals used to regulate plant growth; also produces the amino acid D-alanine
Gibberella fujikuroi	fungus	fungal pathogen of rice		could be used to produce gibberellic acid in quantity for use as chemical plant growth regulators
Fusarium (various species)	fungus	can infect bananas grasses, and flax		can be used to produce various kinds of commercial oils
Corynebacterium michiganense	bacterium	causes canker of tomato	$.2 million (tomato)	
Venturia inalqualis	fungus	causes apple scab		

Note: This is not an exhaustive compilation and is a working list rather than a complete history of microbes in use or planned for future use.

Source: Data compiled by the Environmental Policy Institute, Washington, D.C. from: (1) C.G.T. Evans, T.F. Preece and K. Sargeant, "Microbial Plant Pathogens: Natural Spread, and Possible Risks In Their Industrial Use," A study of the necessity, content and management principles of a possible community action, No. 724-ECI-UK, Commission of the European Communities, XII/1059/81-EN.) and (2) U.S. Congress, Office of Technology Assessment, Commercial Biotechnology: An International Analysis, January 1984.

Appendix C

BIOTECHNOLOGY COMPANIES AND ESTABLISHED CORPORATIONS
INVOLVED IN AGRICULTURAL BIOTECHNOLOGY

PLANT AGRICULTURE	ANIMAL AGRICULTURE	CROP & LIVESTOCK APPLICATIONS
Advanced Genetic Sciences, Inc. (CA)	Advanced Genetic Res. (CA)	American Cyanamid (NJ)
Agrigenetics Corp., (CO)	Ambico Inc. (IO)	Abbott Laboratories
Allied Corporation	AmericanQualex (CA)	Amgen(CA)
Amfac	Animal Vaccine Res. (CA)	Biotechnica Int. (MA)
ARCO Plant Cell Research Inst., (CA)	Antibodies, Inc. (CA)	Bio-Tech. Gen. (NY)
Beatrice Foods	Applied Genetics, (NJ)	Centaur Genetics (IL)
Calgene, Inc. (CA)	Atlantic Antibodies (ME)	Dow Chemical (IL)
Campbell Institute for Research & Technology (NJ)	Bethesda Res. Lab (MD)	Enzo Biochem (NY)
Cargill	Bio-Con Inc. (CA)	W.R. Grace (MD)
Cetus Corp. (CA)	Biogen, Inc. (MA)	H.J. Heinz Co.
Ciba-Geigy	Biotechnica Int. (MA)	Indiana BioLab (IN)
Crop Genetics International (MD)	Bio-Technology General (NY)	Int. Genetic Sciences Part.(NY)
DNA Plant Technology (NJ)	California Biotech (CA)	Int. Minerals & Chem (IN)
Ecogen (NJ)	Cambridge Biosci. Corp. (CA)	DeKalb AgResearch Inc. (IL)
E.I. du Pont (DL)	Centaur Genetics Corp. (IL)	Molecular Genetics (MN)
Elli Lilly & Co. (IN)	Cetus Corp. (CA)	Monsanto (MO)
FMC Corp.	Chiron Cor. (CA)	Multivac (CA)
Frito-Lay, Inc. (TX)	Diamond Laboratories (IO)	Neogen Corp. (MI)
General Foods Corp (NY)	Diamond Shamrock Corp. (OH)	Pfizer (NY)
Genetics Institute (MA)	Indiana Biolab (IN)	A.E. Staley MFG. (IL)
Hawaii Biotechnology Group, Inc. (HI)	Int. Plant Res. Inst.	Upjohn Co. (MI)
Hilleshog	Lederle Laboratories (NJ)	Worne Biotech, Inc. (NJ)
International Plant Research Institute (CA)	Lipsome Co. Inc. (NJ)	Zoecon Corp. (CA)
Kellogg Co.	Liposome Technology (CA)	
Koppers Co.	Merck & Company (NJ)	
Martin Marietta (MD)	Miles Laboratories (IN)	
Miller Brewing Co. (WI)	Molecular Genetics (MN)	
Nabisco Brands, Inc. (NY)	Monoclonal Antibodies (CA)	
Native Plants, Inc. (VT)	Phillips Petroleum	
Phytogen (CA)	Multivac, Inc. (CA)	
Phyto-Tech Lab (CA)	Neogen Corp. (MI)	
Phyto Dynamics, Inc. (IN)	Norden Laboratories (NB)	
Pioneer Hybrid International Corp. (IA)	Repligen Corp. (MA)	
Plant Genetics, Inc. (CA)	Ribi Immunochem Res. Inc. (MT)	
Rohm & Haas (PA)	Salk Institute Biotech/Ind. (CA)	
Royal Dutch Shell	Schering-Plough Corp. (CA)	
Standard Oil of Indiana (CA)	SDS Biotech Corp. (OH)	
Standard Oil of Ohio (OH)	SmithKline Bechman (PA)	
Stauffer Chemical Co. (CN)	Synbiotex Corp. (CA)	
Sungene Technologies Cor. (CA)	Synergene (CO)	
Universal Foods Corp (WS)	Syngene Products & Res. (CO)	
Union Carbide	Syntex Corp. (CA)	
Xenogen, Inc. (CN)	Syntro Corp. (CA)	
	Unigene Laboratories (NJ)	

Source: Data complied by the Environmental Policy Institute, Wash., DC from various industry reports, newspaper accounts and Congressional Office of Technology Assessment Report, Commercial Biotechnology: An International Analysis (1984).

APPENDIX D

SEED COMPANY ACQUISITIONS, MERGERS & RELATED BUSINESS VENTURES 1968 - 1984

Corporate Owner	Acquisition or Investment	Date	Crop Seed Sold or Speciality
Agrigenetics Corporation Boulder, Colorado			
	Agricultural Laboratories, Inc. Columbus, Ohio	1980	
	Arkansas Valley Seeds, Inc. Rocky Ford, Colorado	1976	native grasses
	Colorado Seed Company Monte Vista, Colorado	1977	corn, sorghum, soybean
	Growers Seed Association Lubbock, Texas (Gro-Agri)	1981	
	Jacques Seed Company Prescott, Wisconsin	1981	corn, soybean, sorghum
	Keystone Seed Company Hollister, California	1981	vegetable
	McCurdy Seed Company Fremont, Iowa	1981	corn, sorghum
	Seed Research Associates, Inc Sun City, Kansas	1977	
	Sun Seeds Bloomington, Minnesota	1979	vegetable
	Taylor-Evans Seed Company Tulia, Texas	1980	lawn, corn, sorghum
	V. R. Seeds, Inc. Plymouth, Indiana	1979	soybean, sorghum
	R. C. Young Seed Company Lubbock, Texas	1978	sorghum

AMFAC			
	American Garden Products Ventura, California	1980	
	Glen Walters Nursery Oregon	1977	
	Select Nurseries California	1977	
	Henry Field Seed & Nursery Shenandoah, Iowa	1980	flower, vegetable, lawn
	Gurney Seeds Yankton, South Dakota	1968	vegetable, flower, corn, lawn
	Western Seed & Supply Ronan, MT	1971	corn, lawn
	Jenco Nurseries Dallas & Austin, Texas	1979	
Anheuser-Busch Companies Inc, S. Louis, MO.	North American Plant Breeders (barley breeding program) Berthoud, Colorado	1982	barley
Archer-Daniels-Midland Co. Decatur, Illinois			
	Farmer City Grain Farmer City, Illinois (subsidiary of Tabor Grain)	1979	corn, sorghum, lawn

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Atlantic Richfield Los Angeles, California	Canyon Seed Company Canyon, Texas	1981	triticale
	Dessert Seed Company El Centro, California	1980	flower, corn, vegetable, lawn, sorghum
George J. Ball Chicago, Illinois			
	Ball Seed Company, Div. Chicago, Illinois		flower, vegetable
	Denholm Seed Division Lockport, California		flower
	Pan American Plant Division Paris, Florida		
	Petoseed Saticoy, California		tomato seed
Barenbrug Holland B. V. (Dutch)	Mt. Emily Seeds Cove, Oregon	1979	lawn
Bayer AG (W. German)	Helena Chemical Co. Memphis, TN.		
Beatrice Foods Chicago, IL.	Dahlgren & Company Crookston, Minnesota	1972	
LaFarge Coppee (French)	Wilson Hybrids, Inc. Harlan, IA	April 1984	hybrid corn and soybeans

Canadian Pacific, Ltd.	Maple Leaf Mills (Can.)	1980	lawn, vegetable, flower, corn, sorghum
	Maxville Feed & Seed (Can.)		
Cargill Wayzata, Minnesota			
	ACCO Seeds Belmont, Iowa Tomaco Genetic Giant	1980	corn, sorghum
	Cargill Research Center Minneapolis, Minnesota		corn, sorghum
	Dorman Seeds		
	Kroeker Seeds (Can.)		
	P-A-G Seeds Minneapolis, MN	1971	
	Lankhart Seed Farms	1984	cotton
	Lockett Vernon, TX	1984	cotton
Celanese New York, NY			
	CelPril, Inc. Manteca, California	1975	
	Joseph Harris Seed Company Rochester, New York	1978	vegetable
	Moran Seeds Salinas, California	1974	vegetable
	Niagara Seeds	1980	
	Nitragin Company Milwaukee, Wisconsin	--	

Ciba-Geigy (Switz & Ardsley, NY			corn, soybean
	Ciba-Geigy Seeds (Can.)	--	
	Funk Seeds International Bloomington, Illinois	1974	
	Hybridex (Can.)	1978	
	Louisiana Seed Company Alexandria, LA	1979	corn, sorghum
	Stewart Seeds (Canada)	1977	
Claeys-Luck (French)	Neuman Seed Company (El Centro, California)	1980	vegetable
Continental Grain New York, New York			corn, sorghum, soybeann
	Hannas, Hannas, & Hannas (Can.)	--	
	Pacific Seeds, Golden Acres (Australian firms, Continental holds contracts with them).	--	
L. Daehnfeldt Odense, Denmark	Pacific Seed Production Co. Albany, OR	1983	forage, vegetable turf, and flowers
DEKALB AgResearch, Inc. DeKalb, Illinois			corn, sorghum
	DeKalb, Canada	--	
	Ramsey Seed Manteca, California	1980	corn, sorghum
	Sensors, Inc.	--	

Diamond Shamrock Dallas, Texas			
	Golden Acres Hybrid Seed Co.	--	
Golden Harvest Seeds, Inc. Bloomington, Illinois (Formed by merger of 6 family-owned seed companies).			corn
	Golden Seed Company, Inc. Cordova, Illinois	1973	corn
	Rob-See-Company Waterloo, Nebraska	--	
	Sommer Brothers Seed Company Pekin, Illinois	--	corn, soybean
	Garwood Seed Company Stonington, Illinois	--	corn
	Thorp Seed Company Clinton, Illinois	--	corn
	Columbiana Seed Company Eldred, Illinois	--	corn, sorghum soybean
Hilleshoeg/Cardo (Swedish)	International Forest Seeds Birmingham, Alabama	--	
International Multifoods Minneapolis, Minnesota			
	Guildersleeve Seed Company Hudson, Illinois	1977	
	Lynk Brothers & Baird, Inc. Marshalltown, Iowa	March 1976	corn, sorghum

International Seeds, Inc. Halsey, Oregon			Lease
	North American Plant Breeders (Burlgreen Division only)	---	corn, vegetable, lawn sorghum, soybeans
ISU New York, NY			
	W. Atlee Burpee Company Warminster, PA	1978	vegetable, flower lawn
	G.H. Scott & Sons Marysville, Ohio	1971	lawn
Kay Corporation New York, NY			
	Pacific Oilseeds	1980	corn, sorghum
	Midland Carrollton, Texas	1976	sorghum
Kent Feeds, Inc. Muscatine, Iowa			
	Morton & Sons Seeds, Inc. Sumas, California	1971	
	L. Teweles Seed Company Milwaukee, Wisconsin	1971	
Kirkpatrick-Johnson Associates (Del Mar Division)			
	Delaware (Cont. w/Sandy)		
	Coburn Hodges[illegible] and Co.	1978	corn, sorghum, soybeans
	Huntsville, South Carolina		
	Del Monte		
	Delaware[illegible] Maryland (Cont.)		

Limagrain (French)			
	Ferry Morse	1981	flower, corn, vegetable lawn, sorghum, soybean,
Loft's Pedigreed Seed Bound Brook, New Jersey	Great Western Seed Company Albany, Oregon	--	lawn
Lubrizol			
	Sigco Research, Inc. Breckenridge, MN	1982	hybrid sunflower
	Lynnville Seed Co. Lynnville, IA	Jan 1984	soybean
Mid-Western Nurseries Talequah, Oklahoma	Mt. Arbor Nurseries		
Monsanto St. Louis, Missouri			
	DEKALB AgResearch Inc.'s hybrid wheat program	1982	
	Jacob Hartz Seed Company (through Hybritech Seed International Inc.)	April 1983	
NC + Hybrids Lincoln, Nebraska			corn, sorghum
	Winterset Hybrids Winterset, Iowa	1981	--
	YW Hybrids (Merger) Grand Junction, IA	1983	corn, sorghum, soyeans, alfalfa

Occidental Petroleum Los Angeles, California			
	Ring Around Products Montgomery, Alabama	1978	sorghum, soybean, corn
	Excel Hybrid Products Plainview, Texas	1972	
	Missouri Seed Company Greenridge, Missouri	na	
	Moss Seed Company Little Rock, Arkansas	1972	
	Payne Bros. Seed Company Charlotte, North Carolina	1972	
	Stull Seeds	1975	
	East Texas Seed Company Tyler, Texas	1973	
	West Texas Seed Company	1973	
Rohm & Haas Phil. PA	Coker Pedigreed Seed Co. Hartsville, SC (research partnership called CRSeeds)	1984	to breed soft red winter wheat, soyeans and oats. Rohm & Haas will acquire marketing rights to varieties.
Royal Dutch Shell			
	Olin Plant Breeders	--	
	Rudy Patrick (Part) Mission, Kansas	1974	
	North American Plant Breeders Mission, Kansas (acquired from Olin Corp.)	1983	
	Agripro, Inc.	1973	

	HP Hybrid	na	
	Midwest Seed Growers	1979	
	Tekseed Hybird Tekamah, Nebraska	1974	
Coop de Paul France	Garst Seed Co. Coons Rapids, IA	July 1984	Reciprocal research, testing and marketing agreement
Payco Seeds	Lowe Seed Com. Kankakee, Il.	Sept. 83	
Pfizer New York, New York			
	Clemens Seed Company Beaman, Iowa	1974	soybeans, oats
	Jordan Wholesale Company Cleveland, Missouri	1975	
	Radiologic Sciences	--	
	Trojan Seeds	1973	hybrid corn & soyghum
	Olivia, Minnesota		
	Warwick Seeds (Can.)		
Pillsbury	(See Wicks)		
Pioneer Hi-Bred, Int'l. Des Moines, Iowa			corn, sorghum soybean
	Agricon of Idaho, Inc. Nampa, ID.	Sept. 1974	alfalfa
	Arnold Thomas Research Company. (Fresno, CA.	July 1975	alfalfa
	Nulabs, Inc. Portland, OR	April 1977	microbiology research

	Savage, Minnesota	1973	soybeans
	Pioneer Hi-Bred, Ltd. (Can.)	Nov. 1973	hybrid seed and poultry
R. J. Reynolds Winston-Salem, N.C.	Jackson & Perkins	Oct. 1983	
	Weaver Field Seed Company Grand Rapids, Ohio	1975	
	Bear Creek Corp. , OR	Dec. 1983	garden plants
Purex Lakewood, California			
	Advanced Seeds	na	
	Hulting Hybrids	1977	
Reichold Chemicals White Plains, New York			
	Florida Seed & Feed Oscala, Florida	1979	corn, sorghum, lawn vegetable, soybean
Sandoz Basel, Switzerland			
	Northrup King Minneapolis, Minnesota	1976	flower, corn, lawn vegetable, sorghum,
	McNair Seed Laurinburg, North Carolina	1979	
	Woodside Seed Growers	1974	
	Rogers Brothers Idaho Falls, Idaho	1975	vegetable
	Gallatin Valley Seed Twin Falls, Idaho	--	vegetable
	Sluis en Groot Salinas, California	--	flower, vegetable

	Betaseeds (Can. w/KWS AG)	--	
	Ladner Betaseed (Can.)	1978	
	Pride Seeds , WI		
	National N-K (Can.)	1977	
Klass Pieter Sluis (Dutch)			
	George R. Pedirck & Sons Co. Pedricktown, New Jersey	1981	-
Southwide Memphis, Tennessee			
	Delta & Pine Land Company Memphis, Tennessee	1978	--
	Greenfield Seed Company Harrisburg, Arizona	1979	--
Stauffer Chemical Westport, Connecticut			
	Blaney Farms Madison, Wisconsin	1978	corn
	Prairie Valley Philips, Nebraska	1978	corn, sorghum
	Rauenhorst, Bellows & Assoc.(RBA) Springfield, Illinois	1980	hybrid sunflower
Tate & Lyle	Berger & Plate	na	--
	Seed & Farm Supply, Inc. Liberal, Missouri	1975	

Tejon Ranch (Los Angeles,CA) & Times Mirror (Los Angeles)			
	Waterman-Loomis Company (W-L Research) Bakersfield, California	1974	
Terra Chemicals Int'l. Inc. Sioux City, Iowa			
	Hunt Seed Company Lubbock, Texas	1981	
United Agriseeds, Inc. , Illinois			
	Keltgen Seed Co. Olivia, MN	1982	
	Hofler Seed Company, Inc. Nora Springs, Iowa	1982	lawn, soybean
	DeWine & Hanna Seed Co. Yellow Springs, Ohio	1983	lawn, soybean
Universal Leaf Tobacco Richmond, Virginia			
	Royster Seed Norfolk, Virginia	1980	
Upjohn Kalamazoo, Michigan			
	Asgrow Seed Company Kalamazoo, Michigan	1972	corn, vegetable sorghum, soybean
	Farmers Hybrid Co.(Hybrid Corn Division)	1974	--

	United Hagie Hybrids Des Moines, Iowa	1968	
	Morrison Bros. Seed Co. Spokane, WA.	1983	vegetable
	O's Gold Seed Co. Parkersburg, Iowa	1983 (Sept)	corn, sorghum
Vaughan-Jacklin Downers Grove, Illinois			flower, corn, vegetable, lawn
	Asgrow Mandeville	1977	
	Jacklin Seed Post Falls, Idaho	1981	
	Gold Coast Seed Company Nezpierce, Idaho	1981	--
	Jenks-White Seed Company Tangent, Oregon	1981	lawn
	Michigan State Seed	1973	
VanderHave Rilland, Holland	Interstate Seed Co. Fargo, ND	1984	one of largest producers of hybrid sunflower seed in U.S.
	Interstate SunFlower, Inc. West Fargo, ND	1984	grows & markets edible sunflower foods & birdseed

Weyerhaeuser Co. Tacoma, WA	Wight Nurseries Cairo, GA	1982
	Shemin Nurseries Greenwich, CT	
	Hines Wholesale Nurseries (Western, U.S.)	
Wicks (agricultural unit) San Diego, California	sold to Pillsbury Co.	1982
	M. J. Bean Company, Inc. Wendall, Idaho	1975
	Hunter Bean Twin Falls, Idaho	1975

(115 companies acquired since 1968)

Sources: Data compiled by the Environmental Policy Institute, Washington, D.C. from annual reports of publicly-held corporations; personal interviews with government, industry and university sources; and news reports in the Wall Street Journal, The New York Times, Business Week, Forbes, Seed Trade News, Seedsman Digest, Seed World, and Chemical Week. Other sources include: The F & S Index of Corporate Change; Mergers & Acquisitions; Dun & Bradstreet; Million Dollar Directory; Standard & Poor's Register; Economic Information systems, The Top 1,500 Private Companies, 1981; Ohio State Industrial Directory, 1981; Tennessee Industrial Directory, 1981.

Appendix E

CORPORATE INVESTMENTS, RESEARCH CONTRACTS & JOINT VENTURES
WITH BIOTECHNOLOGY COMPANIES FOR AGRICULTURAL AND RELATED PRODUCTS

Corporation	Biotechnology Company	Date	Potential Agricultural/Food Applications
Abbott Laboratories Chicago, IL	Invested $5 million for a 19% share of Applied Molecular Genetics		unspecified health care products biological pest controls
Agrigenetics Corp. Denver, Co.	----------		owns $2 million Agrigenetics Research Park biotech lab in Madison, WI; advanced research lab in Boulder, CO; and tissue culture lab working on hybrid wheat, soybeans, vegetables and other crops, as well as nitrogen fixation and new seed delivery systems
Allied Corporation	----------		Allied has 40 scientists involved in bioengineering research in agriculture; spending at $30 million annually on ag R & D
----------	Invested $1 million for Calgene, Inc. (CA) (Allied terminated agreement Feb. 1984)		research agreements were for higher plant yields and lower fertilizer requirements

----------	Owns 10% share of Bio-Logicals, Inc., Toronto, Canada		biological control of plant pathogens & yield enhancement research in
----------	$16.5 million, 5 yr. to Genex, Inc.	1983	broad industrial applications
American Cyanamid Co. Wayne, NJ	----------		spends an estimated $70 million annually on agricultural R & D
----------	Spent $5.5 million for 20% equity in Molecular Genetics, Inc.		specified agricultural projects in animal and plant applications.
----------	$1.25 million to Biotechnology General Corp. of New York, NY and Rehovot, Israel	1983-84	to conduct research on bovine, porcine and chicken hormones.
Archer Daniels Midland Company	has collaborative agreement with DNA Plant Technology Corp.		"to test feasibility of growing selected fresh, quality herbs hydroponically, possibly for mass production in a joint venture.
AMFAC	$1.9 million 3-yr. research contract with Hybritech, Inc.	Oct. 83	pharmaceutical products.

Atlantic Richfield Los Angeles, CA	Owns Plant Cell Research Institute, Dublin, CA.		
	Major stockholder in International Genetic Engineering, Inc. (CA)		undisclosed product development agreement.
	Contract with Heinz Co.	1983	to develop high-solids tomato
	Early funding to International Plant Research Institute (IPRI)		
Baxter Travenol Labs	Research agreement with Hybritech, Inc.	Oct. 83	to develop monoclonal antibodies
Beatrice Foods, Inc.	Major stockholder in Int'l Genetic Engineering, Inc. Santa Monica CA.		undisclosed product development agreement
Brown & Williamson Tobacco Corporation	research contract with DNA Plant Technology Corp.	Aug. 1983	biotechnological plant research on tobacco
Campbell Soup Camden, NJ	$9 million cash & $5 million lab & greenhouse to DNA Plant Technology Corp. NJ		working on disease-resistant tomatoes & carrot research
			contract work with Campbells on new tomato varieties
	research contract with Calgene, Inc. (CA)	Sept 1984	for research into developing proprietary high-solids processing tomato varieties with optimum taste, color and texture
	two research contracts with DNA Plant Technology Corp. (NJ)	Sept 1984	for general tomato research and developing fresh market tomatoes with superior characteristics

Cargill Wayzata, MN	----------		working on hybrid wheat, hybrid corn, and hybrid sunflowers
Celanese New York, NY	----------		owns CelPril Industries Research Farm & Bio-Ag Center (CA)
Ciby-Geigy (Switz & Ardsley, NY)	Owns 80% of ALZA Corp. a genetic engineering firm		seed coating, hybrid corn and sorghum
Continental Grain Co. NY, NY.	holds equity in Calgene, Inc.		
Crow's Hybrid Corn Seed. Co.	Research agreement with Sungene	1983	to help Crow's screen its germplasm for high-lysine corn
DEKALB Ag Research Inc., DeKalb, Ill.	Equity position in Bethesda Research Labs, Md. Owns 70% DeKalb-Pfizer Genetics		#2 producer hybrid corn seed
Dow Chemical Midland, MI	----------		spending at least $40 million annually on agricultural R & D; has establishe biotechnology research division; has researched photosynthesis among other projects

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	$5 million research contract with Collaborative Genetics (MA) Also involved with GENEX and Genetech		
DuPont Wilmington, DE	----------		opened a new $88 million Life Sciences research complex in Sept 1984; has made a major commitment to ag biotech research
	Owns New England Nuclear		
	$4.5 million equity invst.; Biotech Research Laboratories, Rockville, MD	1984	to gain options on current and future products
Elf Aquitaine (French)	Research contract with Native Plants, Inc.	1981	tissue culture research on Endod plants for insecticidal compounds and other purposes
Eli-Lilly Indianapolis, IN			Lilly is working in-house to develop and commercialize genetically-made bovine growth hormone; investing $63 million annually (est.) in ag R & D
	Long-term agreement with International Plant Research Institute (CA) Working with Genentech, Inc.		Plant genetics research

Ethyl Corp., Richmond, VA.	Invested $1 million in Biotech Research Labs.		
ADM Corp., Chicago, IL	----------		Doing in-house genetics research in agribusiness
General Foods White Plains, NY	Owns 5% shares of Yogonics		
----------	Participating with 5 other companies in twelve-day biotechnology research at Stanford Univ.		
----------	Contracting research with Calgen Corporation	Since 1979	contract research
----------	5-year, $250,000 research contract with DNA Plant Technology, Inc.	Dec. 1982	"biotechnological plant research"
----------	International Plant Research Institute	March 1983	to develop improved wheat, food processing machines for General Foods
General Mills	"Looking up for genetic industries in agriculture" ANY ARTICLE		
Getty Oil	Owns 34% of Synergen Associates, a genetic engineering firm.		

W.R. Grace	$60 million joint venture with Cetus Madison Corp.; also owns American Breeders Service (WI) leading livestock breeder	June 1984	to develop, manufacture and market biotechnology-based products for agriculture
H.J. Heinz Co.	5-yr. Research Agreement with ARCO's Plant Cell Research Institute	Dec. 1982	high-solids tomato
	3-yr. Research Agreement with Biotechnica Int.	May 1984	"using genetic engineering to develop new processes leading to products of iterest to the food and animal feeding industry."
Hillesog Kabdsjribam, Sweden	owns 14% share of Advanced Genetic Sciences, (AGS) Inc.,	March 1980	
	$268,000 in R & D funding to AGS	1992	to develop new varieties of rapeseed, wheat, & barley
	$307,000 in R & D funding to AGS	1983	" " " "
Hoffman-LaRoche			working to develop genetically engineered bovine growth hormone at its Nutley, NJ research station
IC Industries	Working on single-cell protein called "Pruteen"		
INCO Toronto, ONT.	Invested $12 milion for a 20% share in Biogen; owns equity in Applied Plant Genetics and Immunogen		

International Minerals & Chemical Corp. (IMC) Northbrook, IL	Working with Genetech, Inc.		to develop livestock foot and mouth vaccine; has exclusive marketing rights to the vaccine
	partnership with Biogen NU, Curacao, Netherlands, Antilles		to develop and commercialize genetically-engineered bovine growth hormone Also has exclusive marketing rights to species-specific growth hormones developed by Biogen
Kellogg Company Battle Creek, MI	Invested $10 million in Agrigenetics Corp.		
Kemira OY , Finland	Research contract with Calgene, Inc. (CA)	Nov. 1983	to develop herbicide-resistant varieties of turnip rape
Koppers Company Pittsburgh, PA	Invested $25 million for a 45% share of Genex Corp.		
	Owns 5.8% of Engenics		
	Invested $1.7 million in DNA Plant Technology Corp.	1982	also conducting biotechnological plant research for Koppers
	Formed joint venture with DNAP	Feb. 1984	To develop & commercialize diagnostic kits for plant and agriculture-related diseases.
John Labatt, Inc. , Canada	owns 30% share of Allelix, Inc. Mississauga, ONT.	1981	

Lubrizol Corp.	Invested $25 million in Genentech and is the largest stockholder of the firm with 20% share.		
Martin-Marietta Corp. Bethesda, MD	$25 million in 3 biotech. firms: Molecular Genetics, Inc. ($11.9 million-21% share of company.		developing corn hybrids and and animal health care products.
----------	Chiron Corp. (San Francisco) between 10-20% of company		Produces vaccines, viral diagnostic products & hormones for human & animal health care.
----------	Native Plants, Inc. (Salt Lake City). Between 10-20% of co.		Modify crops, trees and soils to improve plant varieties.
Merck & Co.	----------		Investing $24 million annually (est.) in agricultural R & D, with some work in plant genetics
Monsanto St. Louis, MO	Research agreement with Biotechnica International, Inc.	Oct. 83	To develop genetically-engineered Bacillus Subtilis systems for the expression of of proteins.
	$20 million in Biogen (Swiss).		
	Owns 30% of Collagen		
	Has equity in Genentech, and several research contracts and joint ventures..		is using Genetech's expression systems for testing and marketir

	Owns 10% share of Genex and along with Emerson Electric has invested $10 million in Genex		
	3 yr. agreement with Biotechnica Int.	May 1984	"using genetic engineering manufacture a pesticide candidate for use on field crops"
Nabisco Brands, Inc.	Research joint venture with Cetus Corporation, Emeryville, CA called "Nabisco/Cetus Food Biotechnology Research Partnership"	Feb. 1984	To develop new enzymes for use in food processing and to explore other applications of biotechnology in the food area.
National Distillers & Chemical	Invested $5 million for a 16% share in Cetus Corp.		Research covers use of recombinant DNA in improving microorganisms used in the fermentation of alcohol.
Nestle S.A. Basel, Switzerland	joint research program with Calgene, Inc. (CA) through subsidiary Nestec	April 1984	to develop herbicide-tolerant varieties of soybeans
Pepsi Co. Purchase, NY	----------		Owns Frito-Lay which is using tissue culture & cloning to produce disease resistant potatoes.
Pfizer New York, NY			Investing $22 million (est.) in ag. R & D
	Owns 30% DeKalb-Pfizer Genetics		Genetic research on soybeans sorghum, hybrid corn

Philips Petroleum Co. Bartlesville, OK	37% interest ($10 million) in Salk Institute Biotechnology/ Industrial Associates, Inc. (SIBIA) CA. Owns Phillips Provesto Corp.		methods to improve oil and gas production and gas production and agricultural methods Working on single cell protein
Pioneer Hi-Bred, Int. Des Moines, IA	Established Microbial-Genetics Division,	1982	#1 hybrid corn seed producer in world, working on hybrid wheat
Purex Lakewood, CA	16% interest in Cetus Corp.		
Rohm & Hass Philadelphia, PA	Invested $7 million for ownership in Advanced Genetics Science (CT) and spent $5 million to fund agricultural research including hybrid seed activities at AGS.		Working on chemical hybridizer for wheat
Rhone-Poulenc Agrochimie Lyon, France	Research contract with Calgene, Inc. (CA)	June 1984	to develop new varieties of sunflower tolerant to the herbicide Bromoxynie
Royal Dutch Shell	Has research contract with Celltech; "has a growing interest in plant breeding and what genetic engineering might offer here." (Financial Times 11/27/81) Has equity in Cetus Corp.		Plant genetics

Schering-Plough Kenilworth, NJ	Invested $8 million for a 13% share of Biogen with first rights to any Biogen project in human and animal health care.		Animal health products
Smith-Kline Corp. Philadelphia, PA	Joint venture with Cetus		to develop vaccine for farm animals through rDNA
A.E. Staley Mfg. Co. Decatur, Illinois	Holds 40% share of Bio-Technical Resources, Inc. of Manitowoc, WI.		genetic engineering pertaining to products from corn, soybeans and other renewable resources
Standard Oil of California (Chevron)	Invested $14 million for 17% share of Cetus Corp. Also with Cetus, projects that include a joint venture on production of high-quality fructose through enzymes.		Application of genetic eng. to use of ag. chem & fertlizer.
Upjohn Kalamazoo, MI	Moving into tissue culture work; investing $26 milion (est.) in agricultural R & D		soybean hybrids, vegetables
	Joint venture with Amgen, Inc., of Thousand Oaks, CA	1983	to develop and commercialize genetically-engineered bovine growth hormone
Standard Oil of Indiana (AMOCO)	21% interest in Cetus Corp. working on fertilizers with Cetus.		
Standard Oil of Ohio (SOHIO) Cleveland, OH			"Building a research group for increasing plant productivity" (Science, 9/18/81)

Stauffer Chemical Co. Westport, CT	Owns de Guigne Technical Center (CA); where "research efforts have been accelerated in genetic engineering of plant life".		Increasing crop yield in corn, sorghum & soybeans, biological pest controls.
Terra Chemicals Int'l. Inc. Sioux City, IA			Plant growth regulants
Union Carbide			Investing $46 million (est.) in agricultural R & D; working on plant growth regulants
Wisconsin Alumni Research Foundation Madison, WI	$3 million investment in Cetus Madison Corp.	Nov. '82	Agricultural R & D
Crown Zellerbach Corporation	research contract with Native Plants, Inc.	1981	tissue culture research on Alder (Alnus Rubra tree from Pacific Northwest clonal propagation.

Note: This compilation of joint ventures between corporations and biotechnology companies for agricultural and related products is a representative listing. Other joint ventures are also underway.

Source: Compiled by the Environmental Policy Institute, Washington, D.C. from chemical industry publications, corporate prospectuses and reports, and conversations with industry officials.

TESTIMONY OF JEREMY RIFKIN
BEFORE THE U.S. SENATE COMMITTEE
ON ENVIRONMENT AND PUBLIC WORKS

HEARINGS ON THE POTENTIAL CONSEQUENCES
OF GENETIC ENGINEERING

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STATEMENT BY JEREMY RIFKIN

My name is Jeremy Rifkin and I am president of the Foundation on Economic Trends. In order to undertake a thoughtful examination of the potential environmental impacts of the biotechnical revolution, it is first essential to place this technology within a historical context. With genetic engineering, we begin the process of reorganizing our entire relationship to natural systems. In sheer scope and magnitude, the genetic engineering revolution closely parallels the revolution in fire technology which has established the framework for our traditional approach to nature. For thousands of years we have been burning, soldering, forging, heating and melting the earth's crust, transforming inert materials into new shapes, combinations and forms. We have produced steel, glass, cement, cinnabar and synthetics using fire or pyrotechnology. Now, with the use of genetic engineering technology, biologists are able to recombine genetic material from unrelated species and in so doing, create modified and novel forms of life that have never previously existed in nature. The transition from the age of pyrotechnology to the age of biotechnology raises fundamental environmental questions, some of which I would like to briefly outline.

First, genetically engineered products differ from petrochemical products in several important ways. Because they are alive, genetically engineered products are inherently more unpredictable than petrochemical products in the way they interact with other living things in the environment. Consequently, it is much more difficult to assess all of the potential impacts that a biotechnical product might have on the earth's ecosystems.

In addition, genetically engineered products reproduce, grow and migrate. Unlike petrochemical products, it will often be difficult or impossible to constrain them within a given locale. Finally, once released, it is virtually impossible to recall living products back to the laboratory, especially those products that are microscopic in nature. For all these reasons, genetically engineered products pose even greater long-term potential risks to the environment than petrochemical products.

In the coming decades, it is more than likely that industry will introduce thousands of new genetically engineered products into the open biosphere each year just as industry has introduced thousands of petrochemical products into the environment each year. While many of these genetically engineered organisms will prove to be benign, sheer statistical probability suggests that a small percentage will prove to be dangerous and highly destructive to the environment. In fact, the long-term cumulative impact of thousands upon thousands of introductions of genetically modified organisms could well eclipse the damage that has resulted from the wholesale release of petrochemical substances into the earth's ecosystems.

Secondly, genetic technology, as it is applied in the fields of agriculture and animal husbandry, is designed to increase the speed of maturation and gross productivity of plants and animals beyond the limits imposed by solar production and natural recycling. The objective is to transform biological materials into useful products in an ever accelerating production tempo.

The great myth of the emerging genetic engineering revolution in agriculture is that the ever accelerating production of living products can be successfully managed without ever exhausting the reservoir of life support systems that are essential for maintaining the reproductive viability of living organisms in the future. The point is, living resources are as finite and depletable as fossil fuels.

For example, let us take the case of attempts to genetically engineer new plants that could absorb greater sunlight and increase the rate of photosynthesis. While the benefit of such a procedure seems apparent at first glance, a closer examination reveals the price that would have to be paid to achieve the desired results. Increased photosynthesis would require a greater use of soil nutrients, thus threatening the further depletion and erosion of an already endangered agricultural soil base. Soil depletion and erosion is one of the major problems in modern agriculture today. Attempts to genetically engineer increases in speed of maturation and gross

productivity will place additional burdens on an already overtaxed soil structure, thus posing the very real danger of inadequate nutrient reserves for sustaining future agricultural crops.

Thirdly, transferring genetic traits from one species into the permanent hereditary code of another species poses grave long-term environmental dangers and raises fundamental moral questions. Recombinant DNA techniques allow researchers to cross species boundaries, violating a basic ecological principle. Mating walls in nature maintain the biological integrity of each discrete species and establish a context for stable interaction between species. Without well defined mating walls, nature would cease to exist. Recombinant DNA provides a tool for bypassing species boundaries. It is now theoretically possible, and in some cases, practically possible, to transfer genetic traits between totally unrelated species. The long-term cumulative impact of imposing foreign genetic material into the hereditary blueprint of a species could well lead to serious health problems for each succeeding generation of that species and could ultimately result in the extinction of the species.

Then there is the ethical issue raised by the transfer of genetic traits between species. Imposing foreign genes into the hereditary blueprint of a species violates the telos or integrity of each creature. This represents the most cruel form of treatment as it robs each species of their unique genetic make-up. Transferring traits between species demonstrates a total lack of regard for the principle of species borders, a principle woven into the very fabric of biological and ecological systems.

For all the above stated reasons, it is my opinion that attempts to genetically engineer microbes, plants and animals is tantamount to playing ecological roulette. The earth's ecosystems are complex, highly synchronized and finely balanced. Are we wise enough and smart enough to begin the process of redesigning the blueprints of living systems without destroying the very foundations of the earth's environment?

I find it ironic that government agencies and Congress have limited the debate of genetic engineering to the question of how to proceed and how to regulate. Why is it that virtually no attention has been given to the question of whether, in fact, we should proceed at all with this radical departure in the way we organize and relate to the rest of the living kingdom? Genetic engineering raises the most important social policy question that the human family has ever had to face. Do we begin a long journey over the next several hundred years in which we increasingly become the designers and architects of life itself? Would it not be more prudent at this stage to begin with a spirited public debate on all the benefits and costs of embarking on such a revolutionary change in the way we conceptualize our existence? It is a sad commentary on the nature of our political process that the governmental powers are more than willing to legitimize the full scale application of this technology into the economic and social life of our society even before the citizenry has had the opportunity to be fully informed of the many issues raised by this emerging technological revolution. How can the public advise their elected leaders of their will in regard to the many issues raised by genetic engineering technology when they have not yet been informed of the short and long-term implications of engineering and introducing genetically modified living products into the environment?

When it comes to the question of regulation, the first order of business is to ask whether a "science" exists by which to judge the risk of introducing genetically engineered products into the environment. While we have a science of toxicology for judging the risk of introducing petrochemical

products, we have not yet even attempted to develop a set of scientific protocols and a methodology to ascertain the risks involved in introducing genetically modified organisms into the biosphere. In the absence of a predictive ecology methodology, it is foolhardy to even entertain the idea of regulation. Afterall, how can an agency regulate when no scientific procedure exists to judge the potential risk of genetically engineered products? It is possible that, in the final analysis, a risk assessment methodology might be impossible to establish. If that turns out to be the case, I, for one, believe that we have a responsibility to take the more conservative and responsible course of action -- to reject the introduction of any genetically engineered products into the environment.